

UPPER LIMB

BONES													
Clavicle	<ul style="list-style-type: none"> ▪ Collar or beauty bone, a type of long bone connecting Upper Limb & Thorax. ▪ MC fractured bone in the body overall, the typical site of fracture is the middle third. ▪ The fracture usually occurs because of a Fall on the shoulder or outstretched hand. ▪ The first bone to ossify in intrauterine life. Ossifies by Membranous Ossification ▪ The only long bone that is placed horizontally in the body. ▪ The most common fracture during delivery and labour is a clavicle fracture. ▪ Costoclavicular Ligament: Clavicles Transmit weight of Upper Limb through these. ▪ Coracoclavicular Ligament: Clavicles receive weight of Upper Limb by these. 												
Scapula	<ul style="list-style-type: none"> ▪ A flat triangular bone. ▪ The Inferior angle of the scapula is located at T7 / T8 level (T7 especially) ▪ Scapula attach to the thoracic wall by Serratus anterior muscle, injury to this muscle or its nerve Supply will cause winging of scapula (Long thoracic nerve lesion) ▪ supraglenoid tubercle is located superior to the glenoid cavity and is the site of Attachment for the long head of the biceps Brachii muscle. ▪ The distance by which two touch stimuli must be separated to be perceived as two Separate stimuli is greatest on the back of the scapula. ▪ Two-point discrimination is highest at fingertip and lips and lowest at back. ▪ In two-point discrimination, the mechanism involved is lateral inhibition (increase Contrast between the active receptive field and the inactive neighbours) 												
Humerus	<ul style="list-style-type: none"> ▪ Begins to Ossify at 14th wk. Intrauterine. ▪ Humerus/funny bone is the longest bone of upper Limb. <table border="1"> <thead> <tr> <th>Fracture site</th><th>Structures damaged</th></tr> </thead> <tbody> <tr> <td>Anatomical neck</td><td>Radial nerve</td></tr> <tr> <td>Surgical neck</td><td>Axillary nerve and Posterior Circumflex humeral artery</td></tr> <tr> <td>Spiral groove</td><td>Radial Nerve + Profunda Brachii artery</td></tr> <tr> <td>Supracondylar</td><td>Median nerve damage (e.g., fall from Bicycle)</td></tr> <tr> <td>Medial epicondyle</td><td>Ulnar nerve damage + ulnar collateral artery</td></tr> </tbody> </table> <ul style="list-style-type: none"> • Mainly axillary, radial & ulnar nerve are injured. • Blood supply of Head of Humerus: Arcuate > anterior circumflex artery • Blood supply of Neck of Humerus: anterior & posterior circumflex artery 	Fracture site	Structures damaged	Anatomical neck	Radial nerve	Surgical neck	Axillary nerve and Posterior Circumflex humeral artery	Spiral groove	Radial Nerve + Profunda Brachii artery	Supracondylar	Median nerve damage (e.g., fall from Bicycle)	Medial epicondyle	Ulnar nerve damage + ulnar collateral artery
Fracture site	Structures damaged												
Anatomical neck	Radial nerve												
Surgical neck	Axillary nerve and Posterior Circumflex humeral artery												
Spiral groove	Radial Nerve + Profunda Brachii artery												
Supracondylar	Median nerve damage (e.g., fall from Bicycle)												
Medial epicondyle	Ulnar nerve damage + ulnar collateral artery												

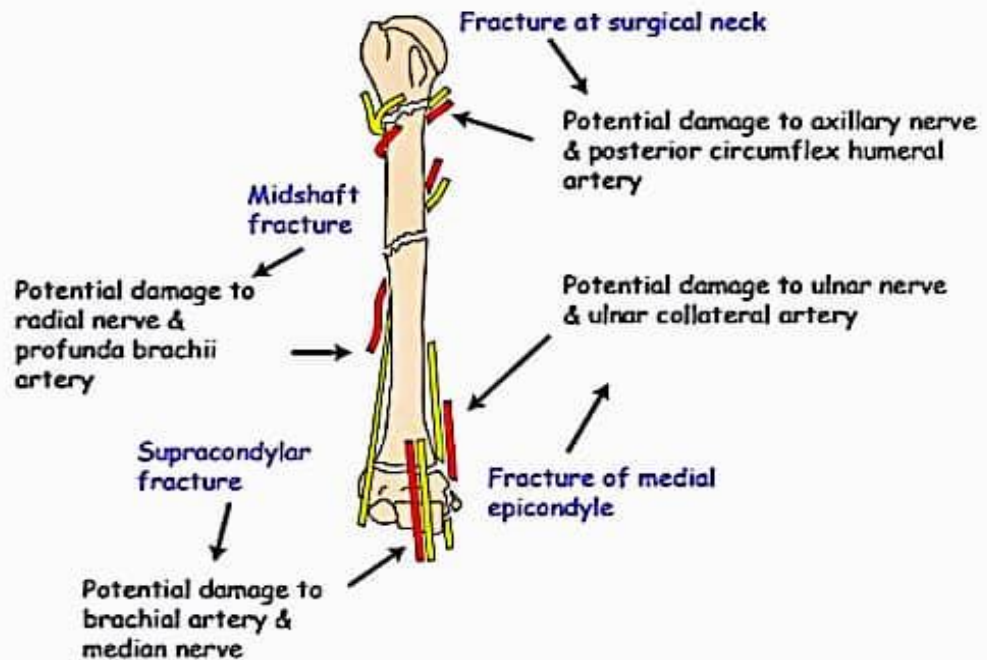
Radius & Ulna

- Radius is Lateral while ulna is medial bone in elbow. **Most common fractured in upper Limb: Radius > Ulna**
- Radial head subluxation occurs in children most commonly, rare in adults.

Fracture	Description
Galeazzi (GR)	○ Fracture of Radius with dislocation of distal radioulnar joint.
Monteggia (MU)	○ Fracture of Ulna with dislocation of radial head.
Colle's fracture (OR) dinner fork deformity	<ul style="list-style-type: none"> ○ Fall on outstretched hand leads to fracture of Distal radius that becomes dorsally displaced, dorsally flexed & angulated. ○ Treat with closed reDuction + cast (CooleD)
Smith fracture (OR) reverse Colle's	○ Fall on flexed wrist leads to forward(volar)/ anterior displacement of distal end of radius. Treated by Closed reduction or ORIF.
Night stick fracture	○ Ulnar shaft fracture while taking defensive position (ward off a stick / Blow).
Green stick fracture	○ Incomplete fracture in a young bone, involving cortex of one side while other side is intact

The Dorsal displacement of distal radius is Colle's fracture whereas reverse (anterior) in smith fracture.

ARTERIES AND NERVES LIABLE TO DAMAGE AT 4 SITES OF FRACTURE OF THE HUMERUS



Colles' Fracture

The result of a fall onto an out stretched hand.



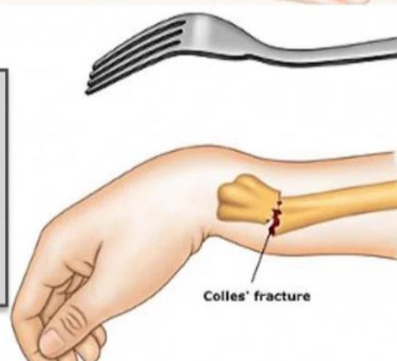
Smith's Fracture

Commonly the result of a fall onto a flexed wrist.



It is commonly taught that Colles' fractures have a "Dinner-fork deformity" which is fairly meaningless.

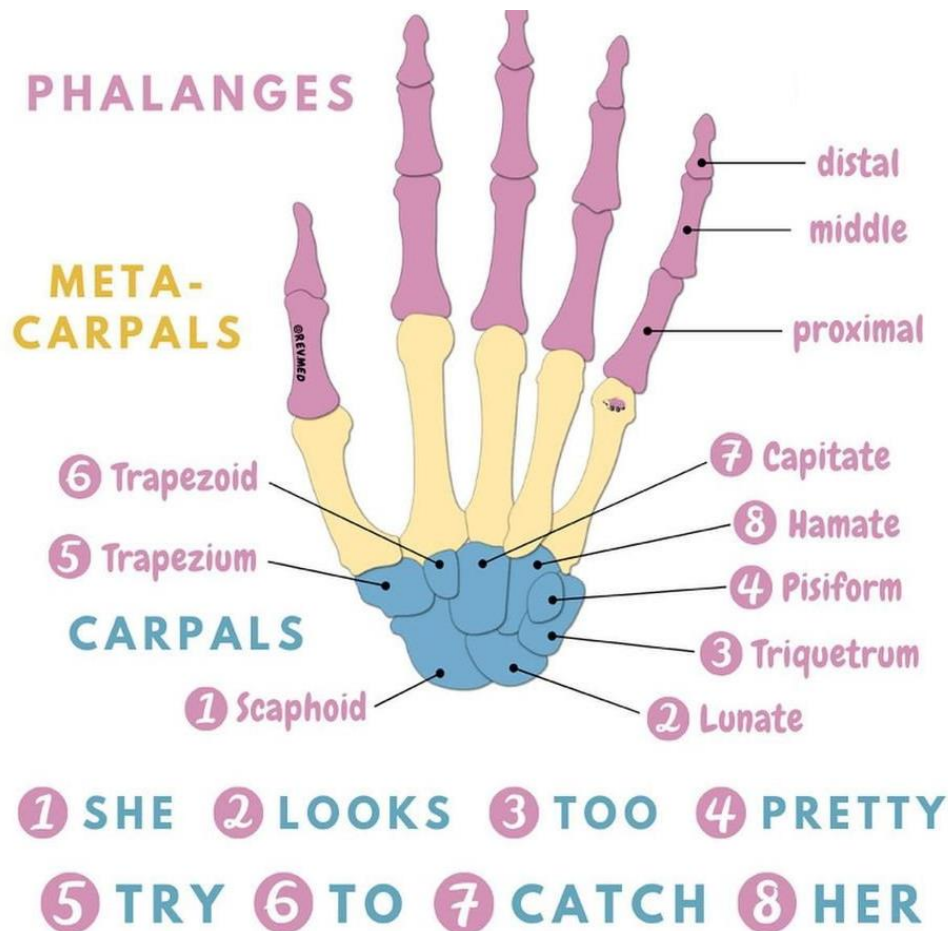
Though it can have meaning if you remember that the "D" in dinner-fork stands for "Dorsally Displaced".



HAND

(8 Carpals, 5 metacarpals, 14 phalanges)

Carpal Bones (Mnemonics: She Looks Too Pretty, Try To Catch Her)	
Proximal Row (she looks too pretty)	Distal Row (Try to catch her)
<p>From lateral to medial and when viewed from anteriorly, consists of:</p> <ul style="list-style-type: none"> The boat-shaped Scaphoid, The Lunate (crescent shape) The Three-sided Triquetrum bone, Pea-shaped Pisiform Pisiform: a sesamoid bone in the tendon of flexor carpi ulnaris and articulates with the anterior surface of the triquetrum. The ulnar nerve and artery lie adjacent to pisiform bone. Scaphoid: The commonest carpal bone fractured, the commonest complication of scaphoid bone fracture is non-union (non-Union > avascular necrosis) Radial artery may get injured in Scaphoid fracture. Lunate: the most Dislocated carpal bone, may compress Median Nerve. Avascular necrosis of lunate occurs more than scaphoid 	<p>From lateral to medial and when viewed from anteriorly, the distal row of carpal bones Consists of:</p> <ul style="list-style-type: none"> The irregular four-sided Trapezium bone, four-sided Trapezoid, Capitate has head and Hamate (has hook) The trapezium articulates with the metacarpal bone of the thumb. Capitate is the largest of the carpal bones, articulates with the base of the 3rd metacarpal. The Hamate, which is just lateral and distal to the pisiform, has a prominent hook (Hook of Hamate) on its palmar surface that projects anteriorly. Ulnar nerve may be injured in hook of hamate fracture



JOINTS

Shoulder joint / Glenohumeral Joint

- ❖ Ball and socket joint, Circumduction (Combination of Flexion, Extension, Abduction, adduction) occurs.
- ❖ Most frequently dislocated Joint in the body. It is most unstable antero-inferiorly.
- ❖ Anterior dislocation of Joint – most common, posterior, and inferior dislocation is rare.
- ❖ Humeral head dislocates mostly inferiorly (Note the diff b/w Shoulder dislocation & Humeral head disloc)
- ❖ Axillary Nerve Is Injured in Inferior > Anterior Dislocation.
- ❖ Axillary vessels (Posterior Circumflex humeral artery) are injured in Anterior disloc mostly.

Movement	Muscles involved
Flexion (C5)	Biceps brachii, Ant fibres of deltoid, Pect Major
Extension (C6, C7, C8):	Latissimus dorsi, Post fibres of deltoid, Teres Major
Abduction (C5)	Middle fibres of deltoid, triceps, Supraspinatus muscle <ul style="list-style-type: none"> ❖ 0-15° - Supraspinatus (Suprascapular nerve) ❖ 15-90° - Deltoid (axillary nerve) ❖ 90°-180° - Serratus anterior + Trapezius. <ul style="list-style-type: none"> ○ Serratus ant (Long Thoracic nerve); Trapezius (Spinal Accessory nerve) ❖ Loss of whole Abd: in upper trunk (Suprascapular nerve) and posterior cord (axillary nerve) of brachial plexus injury.
Adduction (C6, C7, C8)	Pect Major, Teres major & minor, Latissimus dorsi.
Medial Rotation (C6, C7, C8)	Infraspinatus, Teres minor.
Lateral Rotation (C5)	Teres major, L. dorsii, subscapularis.

Elbow Joint

A type of Hinge Joint: Other hinge joints in body: Knee, Ankle, Interphalangeal joint

Movements: Flexion (C5, C6), extension (C6, C7, C8), Supination (C6), Pronation (C7, C8)

- ❖ **Flexion:** B's bend the elbow i.e., Biceps brachii, Brachioradialis, Brachialis
- ❖ **Extension:** Triceps (main extensor), Anconaeus
- ❖ **Supination:** Biceps brachii(main), Supinator.
- ❖ **Pronation:** pronator Teres and Pronator quadratus, palmaris longus.
- Supination & Pronation occur at Superior & Inferior radioulnar.
- **Supination is caused by Musculocutaneous & Radial nerve.**
- **Pronation: Median nerve (PM)**
- The long head of the Biceps brachii muscle travels inside the capsule from its attachment to the supraglenoid Tubercle of the scapula

Wrist Joint (Synovial Ellipsoid/ Condylod joint)

Other Ellipsoid are CMC and Metacarpophalangeal joints, Atlanto-occipital joint (Biaxial synovial ellipsoid)

Movements

- ❖ **Flexion: C7, C8:** Flexor carpii radialis + Ulnaris, Palmaris longus.
- ❖ **Extension C7, C8:** Extensor carpii radialis & Ulnaris
- ❖ **Abduction:** Flexor and extensor carpi radialis, Abductor Pollicis longus, Ext Pollicis Longus
- ❖ **Adduction:** Flexor and extensor carpii Ulnaris

- 1st Carpo-metacarpal joint: Saddle type of synovial joint

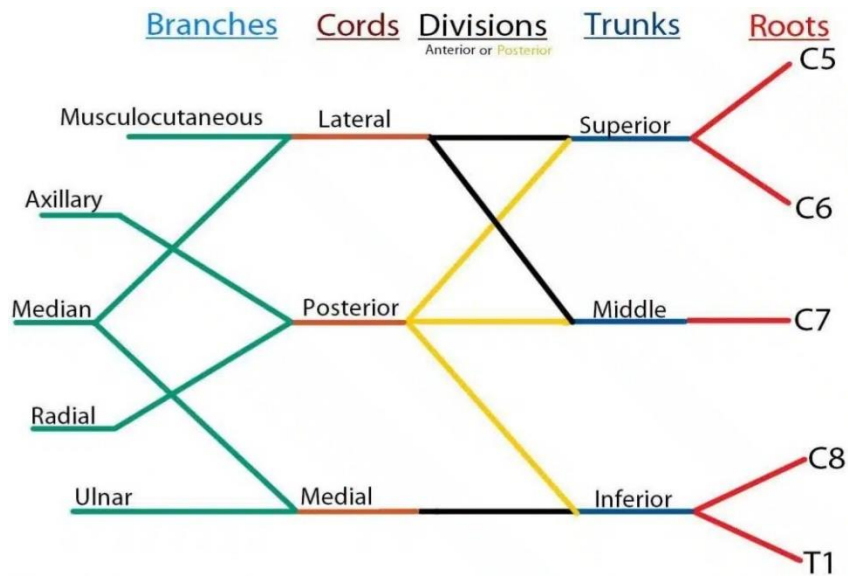
Movements of Fingers	Thumb	Little Finger
<ul style="list-style-type: none"> ➤ Flexion and Extension: By Lumbricals + Interossei ➤ Adduction & Abduction: <div>DAB = Dorsal Interossei -- abduction.</div> <div>PAD = Palmar Interossei -- adduction.</div> <p>1st and 2nd Lumbricals (lateral 2) supplied by Median nerve. 3rd + 4th Lumbricals + Interossei : By deep Branch of Ulnar Nerve</p>	<p>4 muscles (C7, C8 supply)</p> <ol style="list-style-type: none"> 1. Abductor Pollicis brevis 2. flexor pollicis brevis 3. Opponens pollicis all 3 above are supplied by Median nerve. 4. Adductor pollicis: Supplied by deep branch of Ulnar Nerve 	<ul style="list-style-type: none"> ○ Abductor digiti minimi ○ Flexor digiti minimi ○ Opponens digiti minimi ○ All supplied by deep branch of Ulnar nerve.

Rotators cuff Or SITS Muscles	<table><tr><td>Supraspinatus --- abduction</td></tr><tr><td>Infraspinatus --- lateral rotation</td></tr><tr><td>Teres Minor --- lateral rotation</td></tr><tr><td>Subscapularis --- medial rotation</td></tr></table> <ul style="list-style-type: none">• All insert on greater tuberosity except subscapularis which inserts on lesser tuberosity of Humerus.• These muscles support shoulder joint except inferiorly.• Supraspinatus is the only muscle in rotator cuff which causes abduction instead of rotation.• Supraspinatus injury is the Most common rotator cuff injury.	Supraspinatus --- abduction	Infraspinatus --- lateral rotation	Teres Minor --- lateral rotation	Subscapularis --- medial rotation
Supraspinatus --- abduction					
Infraspinatus --- lateral rotation					
Teres Minor --- lateral rotation					
Subscapularis --- medial rotation					
Quadrangular space	<ul style="list-style-type: none">• Contents: Axillary nerve + Posterior circumflex humeral vessels• Boundaries: Superiorly: Subscapularis and capsule of the shoulder joint. Inferiorly: The teres major muscle Medially: The long head of the triceps Laterally: The surgical neck of the humerus				
Cubital fossa	<p>Anterior to elbow is a triangular depression formed between 2 forearm muscles.</p> <p>Boundaries:</p> <ul style="list-style-type: none">• Base: imaginary horizontal line between the medial and lateral Epicondyles.• Medially: Pronator teres• Laterally: Brachioradialis muscle:• Roof: skin, superficial fascia, cephalic vein, Basilic vein, Median cubital vein connecting the Basilic vein and cephalic vein, lateral and medial Cutaneous nerves of forearm• Floor: formed mainly by the Brachialis muscle <p>Contents: from Median to lateral are: MBBR</p> <table><tr><td>Median nerve--most Medial structure</td></tr><tr><td>Brachial artery</td></tr><tr><td>Biceps brachii muscle tendon</td></tr><tr><td>Radial nerve--Most lateral structure</td></tr></table> <ul style="list-style-type: none">• The clinician places the stethoscope over brachial artery in the cubital fossa to take B.P.• The ulnar nerve does not pass through the cubital fossa. Instead, it passes posterior to the Medial epicondyle	Median nerve--most Medial structure	Brachial artery	Biceps brachii muscle tendon	Radial nerve--Most lateral structure
Median nerve--most Medial structure					
Brachial artery					
Biceps brachii muscle tendon					
Radial nerve--Most lateral structure					
Cubital tunnel syndrome	<ul style="list-style-type: none">• Pressure or stretching of the ulnar Nerve (also known as the “funny bone” nerve), which can cause numbness or tingling in the ring and small fingers, pain in the forearm, and/or weakness in the hand.				
Clavipectoral fascia	<ul style="list-style-type: none">• Sheet of connective tissue that is attached above to the clavicle. Below, it is split to enclose the pectoralis minor muscle and then continues downward as a Suspensory ligament of the axilla and joins the fascial floor of the armpit.• During the axillary node clearance for breast cancer, the clavipectoral fascia is incised and this Allows access to the nodal stations. <p>Contents (TLC)</p> <ul style="list-style-type: none">○ Thoraco-acromial artery○ Lateral pectoral nerve○ Cephalic vein				

Brachial plexus

- Brachial plexus is a network of nerves formed by the anterior rami of the Lower four cervical Nerve and first thoracic nerve: **C5, C6, C7, C8, T1**
- **Prefixed plexus:** contribution by c4 is large and T2 is often absent.
- **Post fixed plexus:** lacks C5 but has T2 contribution.
- **Mnemonics for Brachial plexus: Really Tired Drink Coffee Now—Root, Trunk, Division, Cord and Branches**
- Root, trunk, and division is present in the posterior triangle of the neck.
- **Cords are present in the axilla in relation with 2nd part of Axillary artery.**
- No peripheral nerves originate directly from the divisions of the brachial plexus.
- The inferior trunk lies on rib posterior to the subclavian artery; the middle and superior trunks Are more superior in position.
- The six (6) division of brachial plexus unit to form three (3) cords.
- The motor function can be tested by eliciting the movement of the thumb.
- The Ring finger has sensory innervation from radial, median and ulnar nerve.
- A person with Whiplash injury cause damage to C5-C6 will result in loss of flexion of the elbow Joint, which occurs due to any jolt or jerk beyond the range of movement.
- **Superior trunk: C5 and C6**
- **Middle trunk: C7**
- **Inferior trunk: C8 and T1.**
- Each trunk divides into Anterior or ventral division, Posterior or dorsal division.
- **Lateral cord:** Union of anterior division of upper and middle trunk
- **Medial cord:** formed by Anterior division of lower trunk.
- **Posterior cord:** Union of posterior divisions of all three trunks.
- **Branches of Brachial Plexus**
- **Branches of root:** Long thoracic nerve (C5,6,7- nerve to serratus anterior), Dorsal scapular nerve (c5- rhomboids muscle)
- **Branches of trunk (Only from Upper trunk):** Suprascapular nerve (C5, C6 supra and infraspinatus)], Nerve to Subclavius (C5, 6).
- **Lateral cord: (C5,6,7)** Lateral pectoral nerve, lateral root of **median** nerve, **Musculocutaneous** nerve. Remember by **(2LM)**
- **Medial cord (C8, T1): (M4U)**
- Medial pectoral nerve.
- Medial cutaneous nerve of arm
- Medial cutaneous nerve of forearm
- Medial root of median nerve
- Ulnar nerve.
- **Posterior-cord (C5-T1): ULTRA**
- Upper Subscapular (C5,6), Lower Subscapular (C5,6)
- Thoracodorsal nerve (c6, 7, 8- nerve to Latissimus dorsi).
- Axillary nerve (c5,6); Radial nerve (C5-T1).

BP	Parts				
5 Roots	C5	C6	C7	C8	T1
3 Trunks	Upper			Middle	Lower
6 Divisions	3 Anterior		3 Posterior		
3 Cords	Lateral		Posterior		Medial
5 Branches	MC	AXILL	RAD	MED	ULNAR



AXILLARY NERVE (C5, C6)		MUSCULOCUTANEOUS NERVE (C5,6,7)	
<ul style="list-style-type: none"> Supplies Teres minor + Deltoid and the Skin over the lower half of deltoid. Nerve injuries at: <ul style="list-style-type: none"> Anterior dislocation of shoulder joint Sub glenoid displacement of the head of the humerus into quadrangular space Surgical neck fracture cause injury to: Axillary nerve & Posterior circumflex artery 		<ul style="list-style-type: none"> In lower part of axilla lateral to axillary artery enters the front of arm by piercing Coracobrachialis. Passes downward between biceps and brachialis Appears at lateral margin of bicep tendon. It continues down in forearm as lateral Cutaneous nerve of forearm. Supplies Biceps, Brachialis, Coracobrachialis, and elbow joint 	
	MEDIAN NERVE	ULNAR NERVE	RADIAL NERVE
Root value	C5 – T1	C8 – T1	C5 – T1 (longest)
Course	<p>(labourer's nerve / Eye of Hand)</p> <ul style="list-style-type: none"> Arise from Lateral and medial cord of brachial plexus, Down the arm it crosses the brachial artery to reach its medial side. The nerve passes Between the two heads of pronator teres (anterior Interosseous nerve) At wrist it lies behind the tendon of palmaris Longus The median nerve enters the palm by passing behind the flexor retinaculum and through the Carpal tunnel. 	<p>Musicians /funny bone nerve</p> <ul style="list-style-type: none"> Arises from Medial cord of brachial plexus, descends along Medial side of axillary and brachial Arteries up to Coracobrachialis, then pierces, Medial intermuscular septum and enters Posterior compartment of arm. It then passes behind the medial epicondyle of Humerus, enters forearm, passes anterior to flexor Retinaculum, and divides into superficial and deep terminal branches 	<ul style="list-style-type: none"> Arises from posterior cord of brachial plexus, winds around spiral groove of humerus along with Profunda brachii artery. Enters posterior compartment of arm as it descends in front of lateral epicondyle and Divides into superficial and deep branches

Supply	<p><u>Sensory</u></p> <ul style="list-style-type: none"> • Thenar eminence • the lateral 2/3 of the palm • Palmar aspect of lateral 3 ½ fingers • Dorsal fingertips of lateral 3 ½ fingers <p><u>Motor:</u></p> <ul style="list-style-type: none"> • No major branches in the arm • Supplies muscles in the anterior compartment of the forearm i.e., Pronator teres and quadratus, Palmaris longus • Flexor carpii radialis • Flexor digitorum superficialis • Flexor pollicis longus. <p><u>Supply in hand:</u></p> <p>LOAF</p> <ul style="list-style-type: none"> • L- Lateral two Lumbricals • O-Opponens pollicis – Cause opposition of thumb with the little finger • A- Abductor pollicis brevis • F -Flexor pollicis brevis 	<p><u>Sensory</u></p> <ul style="list-style-type: none"> • Hypothenar eminence • Medial 1/3rd of the palm • Dorsal aspect of the medial 1/ ½ fingers • Palmar aspect of the medial 1 ½ fingers • Medial 1/3rd of the dorsum of the hand <p><u>Motor</u></p> <ul style="list-style-type: none"> • Flexor carpi ulnaris • Medial half of flexor digitorum Profundus • Elbow joint • Interossei • Medial two Lumbricals • Adductor pollicis 	<p><u>Sensory</u></p> <ul style="list-style-type: none"> • Superficial branch of radial nerve: predominantly sensory, Supplies posterior arm & forearm. • Lateral 2/3rd of dorsum hand • Proximal dorsal aspect of 3 ½ fingers. <p><u>Motor</u></p> <ul style="list-style-type: none"> • Triceps & anconeus • brachialis • Brachioradialis • extensor carpi radialis Longus • Supinator. <p>The deep branch of radial nerve (posterior Interosseous nerve) is mainly motor, passes b/w heads of Supinator muscle.</p>
--------	--	---	--

Testing Motor Function

- “Thumbs up!” = Thumb Extension = Radial Nerve
- “Okay sign” = Flexor Pollicis Longus + Flexor Digitorum Profundus = Median Nerve

• Normal = Flex both



Abnormal = Unable to



- Thumb Opposition = Opponens Pollicis = Median Nerve
- “Fingers crossed” (Index + Middle) = Ulnar Nerve
- Froment’s Sign = Ulnar Nerve Palsy
= weak Adductor Pollicis
= Flex Flexor Pollicis Longus to compensate to pinch rather than grip

Normal



Froment's positive



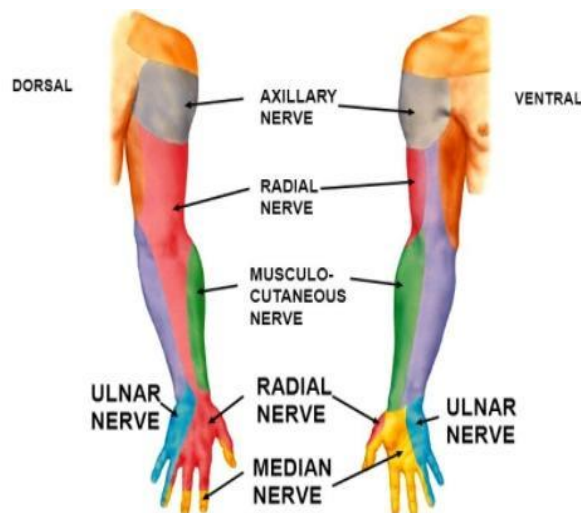
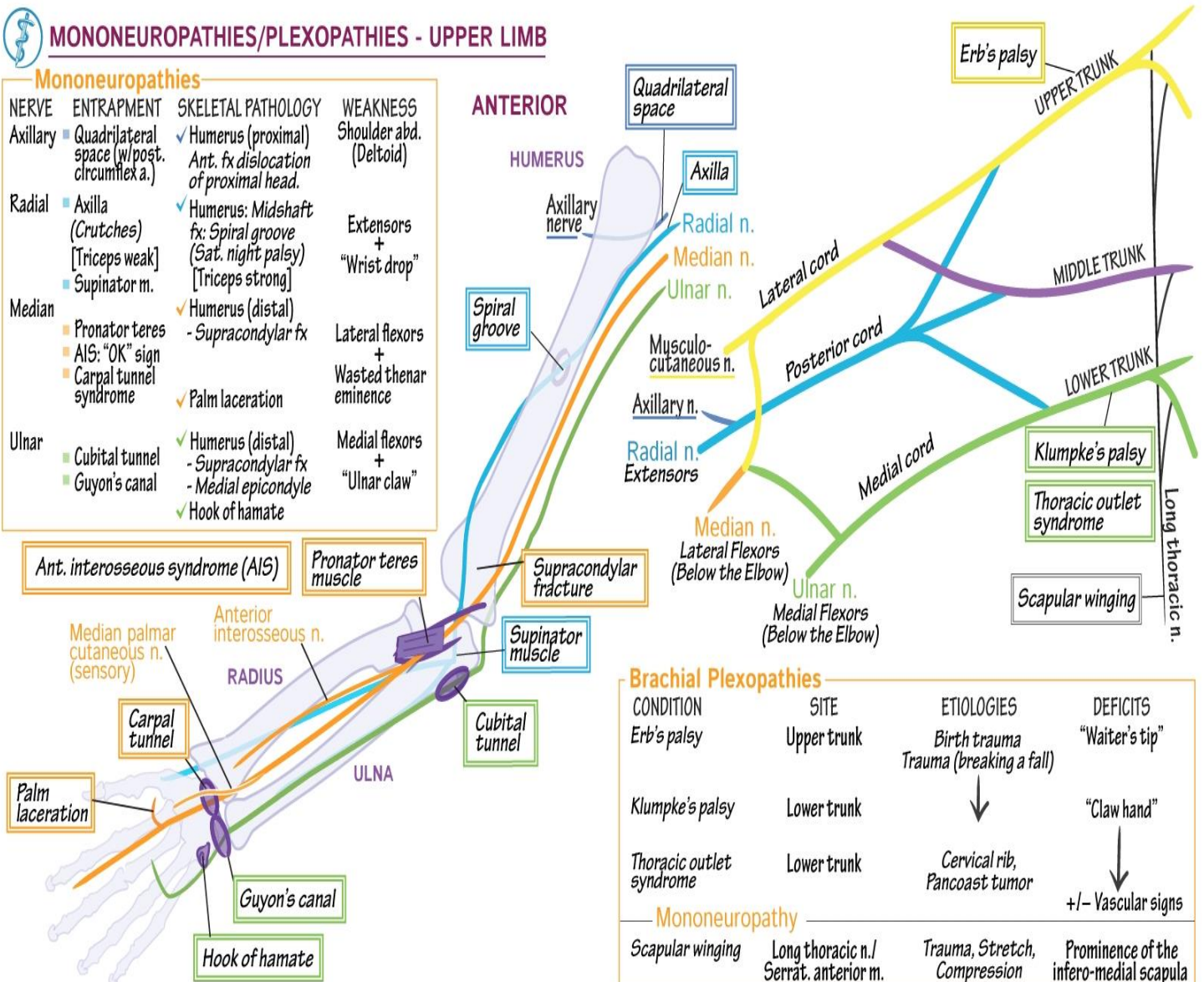
CLINICAL ANATOMY		
Median Nerve	<p>Nerve may be injured at Supracondylar fracture Or Dislocation of lunate or with Injection in the cubital fossa.</p> <p>Injury causes</p> <ol style="list-style-type: none"> 1. Carpal tunnel syndrome: Sensory Loss in the digits > motor supply affected. 2. Pointing index/Ape thumb 3. Loss of abduction of thumb 4. Unable to hold pen / count your finger 	<p>IMP CONCEPTS</p> <p>✓ Proximal Lesions: At Elbow level cause Muscle Wasting & Sensory Loss e.g., Thenar/ Hypothenar wasting.</p> <p>✓ Distal Lesions: At wrist level or below cause Claw hands (Ulnar / Median nerve involved)</p>
Ulnar Nerve	<p>May be injured Behind Medial epicondyle or Lateral to Pisiform</p> <p>Injury causes:</p> <ol style="list-style-type: none"> 1. Claw hand—metacarpophalangeal joints of the fingers are hyperextended, and the interphalangeal joints are flexed because the function of most of the intrinsic muscles of the hand is lost. 2. Total claw: caused by loss of lumbricals. 3. Cubital tunnel syndrome: Ulnar nerve may be compressed in the cubital tunnel formed by the tendinous arch joining the humeral and ulnar head of attachment of the flexor carpi Ulnaris 4. Guyon's canal syndrome: Compression of the ulnar nerve may occur at the wrist where it Passes between the Pisiform and hook of the hamate The compression of the ulnar nerve in this tunnel may result in hypoesthesia in the medial One and a half digits and weakness of the intrinsic muscle the hand 5. Difficulty making fist because of the paralysis of most intrinsic hand muscles. 6. Fromet's sign is +ve in Ulnar palsy 	<ul style="list-style-type: none"> • Injuries of whole nerve causes both motor & sensory loss • while lesion of branches like anterior/ posterior interosseous nerves cause only Motor loss, not sensory Loss. • Anterior interosseous nerve is a branch of Median Nerve (Tested by OK Sign) • Posterior interosseous is a branch of Radial nerve. • APE hand in Median nerve damage • Claw hand for Ulnar • Wrist drop for Radial nerve. • Thenar wasting in Median nerve (C8) damage. • Hypothenar & Intrinsic muscle wasting in Ulnar nerve (T1) damage • Median nerve damage at elbow: Hand of Benediction.
Radial Nerve	<ol style="list-style-type: none"> 1. Injured at Mid shaft Humeral fracture at Spiral groove: Extension is possible because long head of triceps is spared 2. Scaphoid fracture 3. Saturday night palsy refers to a compressive neuropathy of the radial nerve that occurs from prolonged, direct pressure onto the upper medial arm or axilla by an object or surface e.g., Sleeping/ sitting on Chair by arm hanging by the side on chair. 4. Injury causes Wrist drop/ Finger drop (if Posterior interosseous is injured) 	<p>Muscles of hands -- innervation</p> <p>C8 + T1 > Ulnar + Median nerve > T1 > Ulnar Nerve</p>



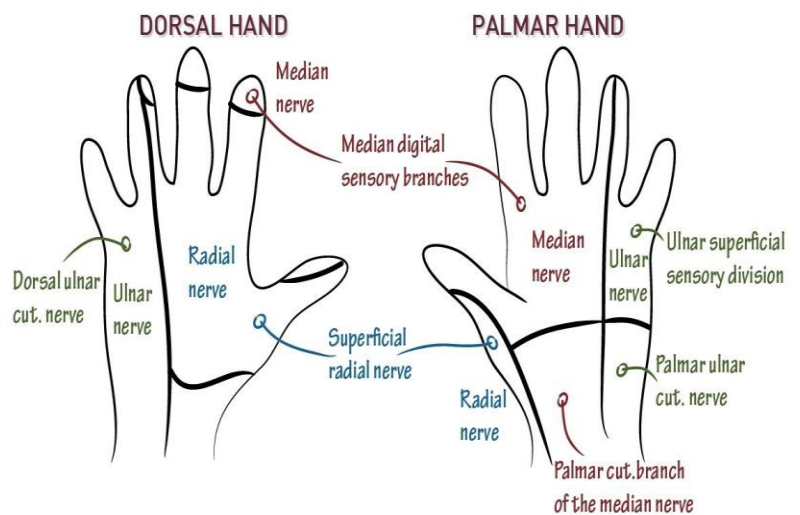
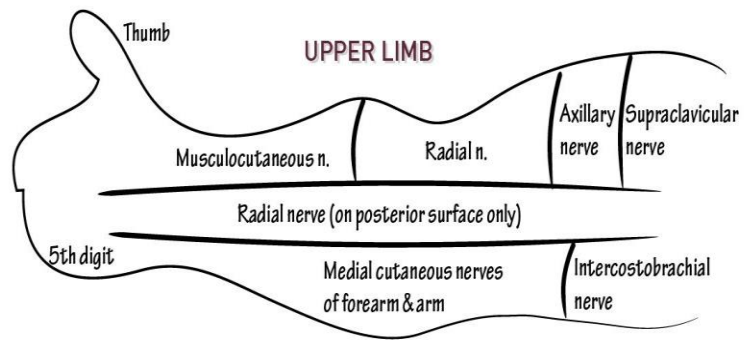
MONONEUROPATHIES/PLEXOPATHIES - UPPER LIMB

Mononeuropathies

NERVE	ENTRAPMENT	SKELETAL PATHOLOGY	WEAKNESS
Axillary	<ul style="list-style-type: none"> Quadrilateral space (w/post. circumflex a.) 	<ul style="list-style-type: none"> Humerus (proximal) Ant. fx dislocation of proximal head. 	Shoulder abd. (Deltoid)
Radial	<ul style="list-style-type: none"> Axilla (Crutches) [Triceps weak] Supinator m. 	<ul style="list-style-type: none"> Humerus: Midshaft fx: Spiral groove (Sat. night palsy) [Triceps strong] 	Extensors + "Wrist drop"
Median	<ul style="list-style-type: none"> Pronator teres ALS: "OK" sign Carpal tunnel syndrome 	<ul style="list-style-type: none"> Humerus (distal) - Supracondylar fx ✓ Palm laceration 	Lateral flexors + Wasted thenar eminence
Ulnar	<ul style="list-style-type: none"> Cubital tunnel Guyon's canal 	<ul style="list-style-type: none"> Humerus (distal) - Supracondylar fx - Medial epicondyle ✓ Hook of hamate 	Medial flexors + "Ulnar claw"



<div> <div></div> <div>SENSORY MAPS - UPPER LIMB</div> </div>		
<div> <div>✓</div> <div>Palmar cutaneous branch of the median nerve is spared in carpal tunnel syndrome (median neuropathy at wrist).</div> </div>		
<div> <div>✓</div> <div>Both the dorsal ulnar cutaneous nerve and palmar ulnar cutaneous nerve branch proximal to Guyon's canal.</div> </div>		
NERVE	SPECIFIC BRANCH	ANATOMIC AREA
MUSCULO-CUTANEOUS	Lateral cutaneous nerve of the forearm	Lateral forearm
RADIAL	Lower lateral cutaneous nerve of the arm	Lower lateral upper arm
	Posterior cutaneous n.'s to forearm and arm	Posterior midline forearm and arm
AXILLARY	Upper lateral cutaneous nerve of the arm	Upper lateral arm
SUPRA-CLAVICULAR	Specific anatomic branches	Shoulder
MEDIAL CUT. N.'S FOREARM & ARM	Supplied by the medial cord brachial plexus	Medial forearm and arm
INTERCOSTO-BRACHIAL N.	Supplied by T2	Axilla



BRACHIAL PLEXUS INJURIES

Erb's Duchenne palsy		Klumpke's paralysis	
Upper trunk: C5 – C6 nerve roots affected		Lower trunk: C8 – T1 affected	
Mechanism of injury: <ul style="list-style-type: none"> Nerve traction or compression Excessive displacement of the head to the opposite side and depression of the shoulder on the same side. Obstetrical injury 		Mech of injury: <ul style="list-style-type: none"> Violent upward pull of the shoulder. Fall on hyper abducted shoulder. Penetrating trauma or tumour Obstetrical traction injury 	
Clinical presentation: Waiter's/Porter's tap position/deformity		Clinical presentation: <ol style="list-style-type: none"> Claw hand position Intrinsic Hand Muscle Weakness and Atrophy (lumbricals Weakness) Sensory loss on Medial Side of the Arm Horner syndrome – ptosis, miosis, anhydrosis. 	
Resultant Position	Weak muscles		
Adducted shoulder	Deltoid, Supraspinatus		
Internally rotated shoulder	Infraspinatus Teres Minor		
Extended elbow	Biceps, brachioradialis		
Pronated elbow	Supinator, brachioradialis		
Flexed wrist	ECRL, ECRB		
Sensory loss on lateral forearm	No Horner syndrome		

ANATOMICAL SNUFF BOX /RADIAL FOSSA

A triangular depression found on Lateral aspect of dorsum of hand- best Seen when the thumb is extended.

Boundaries	
Lateral border	Formed by tendons of the abductor pollicis longus and extensor pollicis Brevis
Medial border	Formed by the tendon of the extensor pollicis longus EPL
Floor	Formed by the scaphoid and trapezium, and distal ends of the tendons of the Extensor carpi radialis longus and extensor carpi radialis brevis
Contents	Radial artery and nerve, Cephalic vein, Scaphoid (forms the floor of snuff box)
Clinical importance	Bleeding from Anatomical Snuff box indicates radial artery injury . Scaphoid can be palpated for fracture assessment.

All flexors pass anterior to flexor retinaculum while extensors pass beneath or posteriorly.

NOTE! Flexor retinaculum is also known transverse carpal ligament.

Structures anterior to flexor retinaculum	Structures posterior to flexor retinaculum
<ul style="list-style-type: none"> ❖ Flexor carpi ulnaris tendon ❖ Ulnar nerve and ulnar artery ❖ Palmar cutaneous branch of ulnar ❖ Palmaris longus tendon ❖ Palmar cutaneous branch of the median nerve 	<ul style="list-style-type: none"> ❖ Median nerve ❖ Flexor digitorum superficialis tendons and Flexor digitorum Profundus ❖ Flexor pollicis longus tendon ❖ Flexor carpi radialis tendon
Structures anterior to Extensor retinaculum	Structures posterior to Extensor retinaculum
<ul style="list-style-type: none"> • Basilic & Cephalic Vein • Superficial branch of radial nerve • Posterior Cutaneous branch of Ulnar nerve 	<ul style="list-style-type: none"> • Extensor carpi ulnaris tendon • Extensor digitorum minimi tendon • Extensor digitorum and extensor indices tendon • Extensor pollicis longus tendon • Extensor carpi radialis longus and brevis tendon • Abductor pollicis brevis and extensor pollicis brevis tendon

BLOOD SUPPLY OF UPPER LIMB**Axillary artery**

- Begins at the lateral part of the first rib behind Pectoralis minor as a continuation of the subclavian artery, ends at the lower border of teres major muscle and continue as the brachial artery.
- During its course via axilla, it is crossed on its superficial aspect by the pectoralis minor muscle Which divides it into 3 parts. The axillary vein is medial to the artery.
- Cords of brachial Plexus are arranged around the 2nd part of the artery (i.e., part deep to the pectoralis minor); the Lateral cord being lateral, the medial cord--medial, and posterior cord behind.

BRANCHES : (6)

1 branch from the first part, 2 branches from the 2nd part, and 3 branches from the third part.

Most of these branches go towards the Walls of the axilla.

- **1st part** → 1 branch, Superior thoracic artery , **Superior** to the Pectoralis minor muscle
- **2nd part**—Two branches : Thoracoacromial artery + Lateral thoracic artery **Posterior** / deep to the Pectoralis minor muscle

Thoracoacromial artery pierces clavipectoral fascia and soon breaks up into 4 branches.

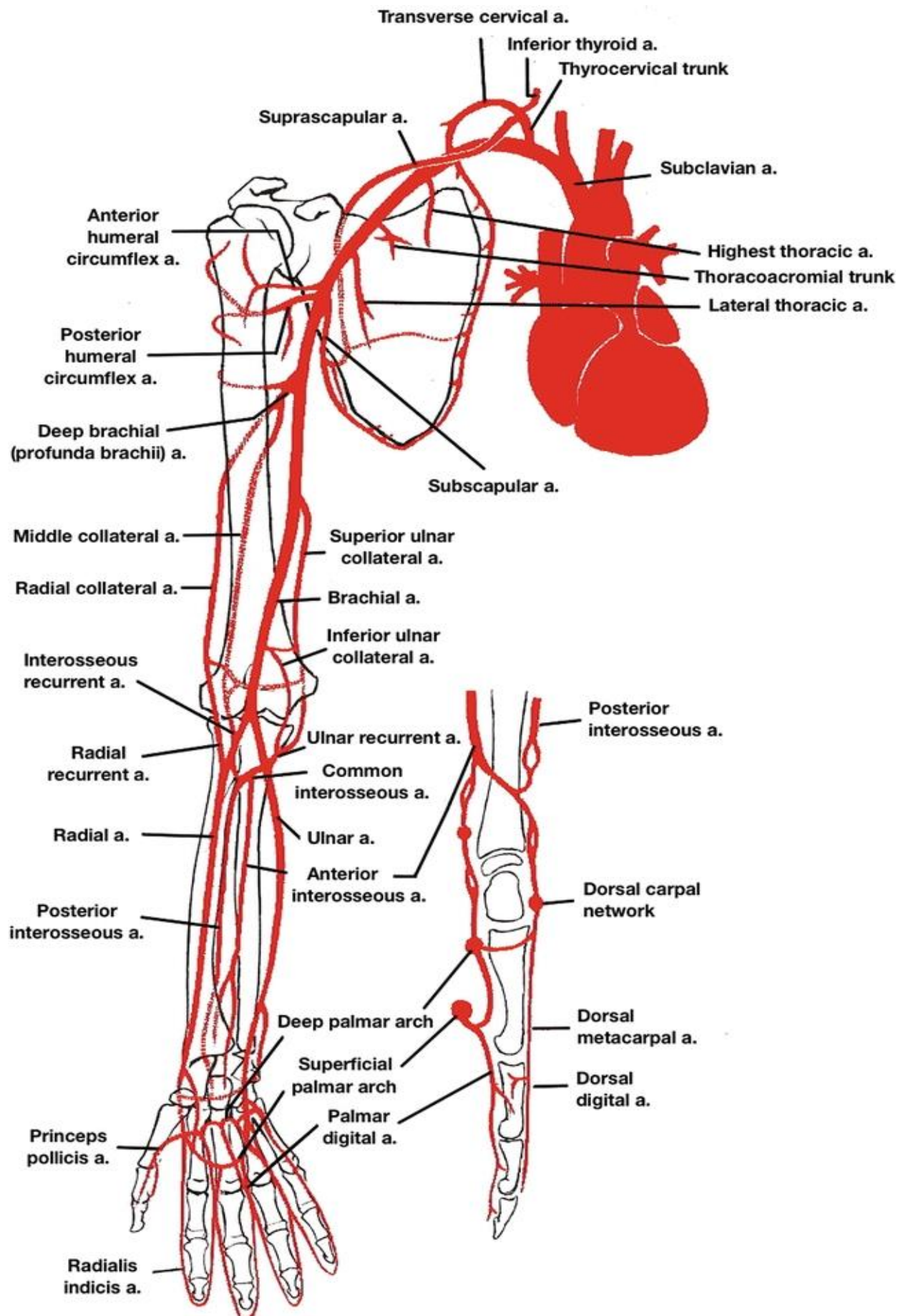
Lateral thoracic artery: In the females, the lateral thoracic supplies breast via its lateral mammary branches.

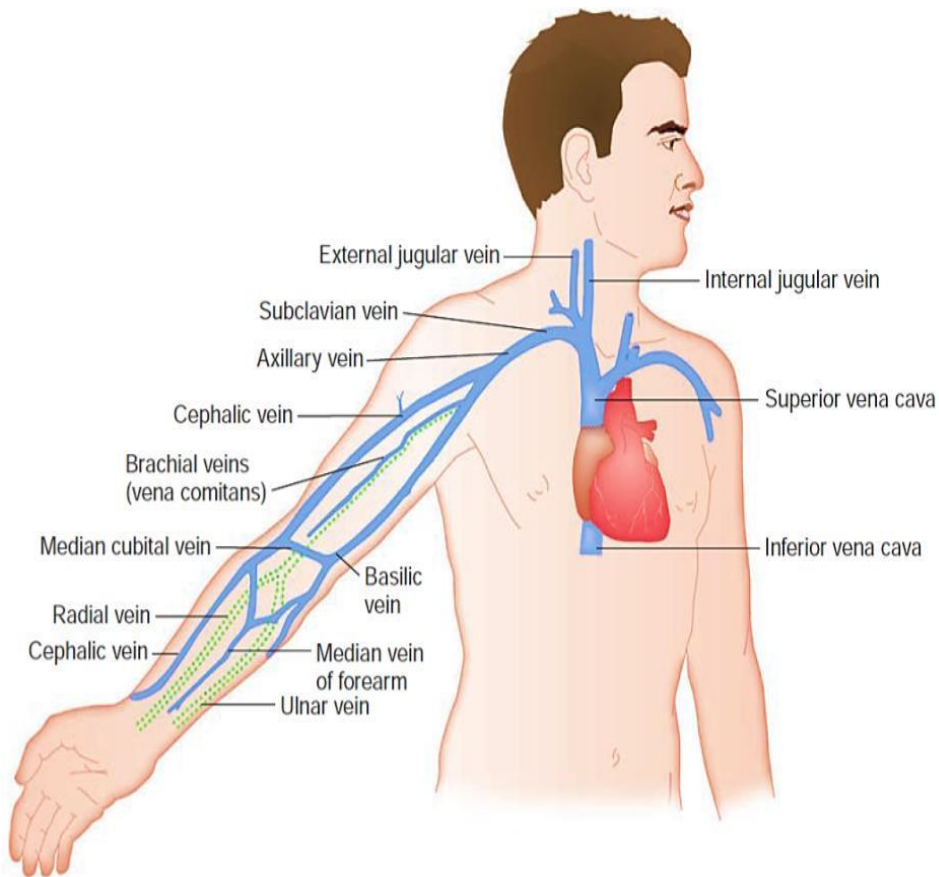
Relations of 2nd part:

- Anteriorly: Pectoralis minor and pectoralis major
- posteriorly: Posterior cord of the brachial plexus
- Laterally: Lateral cord of the brachial plexus
- Medially Medial cord of the brachial plexus and axillary vein

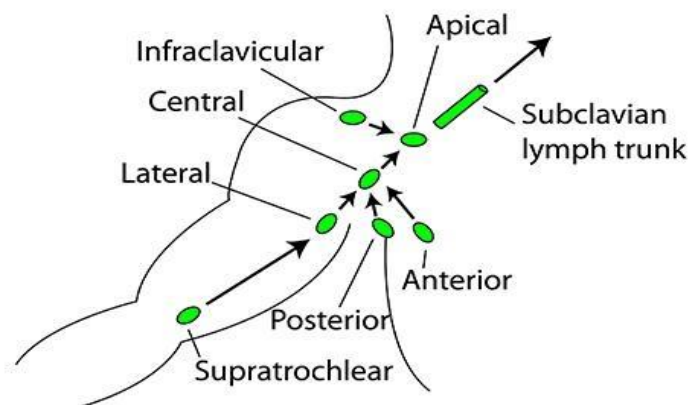
	<p>3rd part gives 3 branches, it is present Inferior to the Pectoralis minor muscle.</p> <ul style="list-style-type: none"> • Subscapular artery—largest branch • Anterior circumflex Humeral artery • Posterior circumflex Humeral artery
Brachial artery	<ul style="list-style-type: none"> ○ Begins as a continuation of the axillary artery at the lower border of the teres major muscle. ○ The artery at first is located on the medial side of the arm in anterior compartment, not present in Axilla. ○ It terminates just distal to the elbow joint where it divides into the radial and ulnar arteries. ○ The course of the median nerve relative to brachial artery in the upper arm is Lateral to anterior to medial. <p>BRANCHES</p> <ul style="list-style-type: none"> i. Profunda brachii artery (largest and first branch): supplies the posterior compartment of the arm. It accompanies the radial nerve to go into the spiral groove on the posterior Surface of the humerus. ii. Nutrient artery to humerus enters the nutrient foramen of humerus located near the Coracobrachialis insertion. iii Superior ulnar collateral artery originates near the middle of the arm and accompanies the ulnar nerve. iv. Inferior ulnar collateral (or supratrochlear artery) :divides into the anterior and posterior branches, which take part in the Formation of arterial Anastomosis around the elbow. V. Radial and ulnar arteries (terminal branches) <p>Clinical importance:</p> <ul style="list-style-type: none"> ❖ Brachial pulse: The brachial pulse is commonly felt in the cubital fossa medial to the Tendon of biceps. ❖ To Stop the bleeding: The brachial artery can be effectively compressed Against the shaft of humerus in the level of insertion of Coracobrachialis to stop the Hemorrhages in the upper limb occurring from any artery distal to the brachial artery e.g. bleeding wounds of the palmar arterial arches ❖ Volkmann's ischemic contracture: Rupture of the brachial artery in supracondylar fracture of the humerus leads to this condition.
Radial artery	<p>Originate at neck of radius and terminates at hand as deep palmar arch. In middle third of forearm radial nerve lies lateral to it, Winds back around lateral aspect of wrist to reach posterior surface of hand.</p> <p>BRANCHES:</p> <ul style="list-style-type: none"> • Muscular branches, Recurrent branch: • Superficial palmar branch joins the ulnar artery to form superficial palmar arch • First dorsal metacarpal artery
Ulnar artery	<p>Continue in hand as superficial palmar arch, enters the hand superficial to flexor retinaculum lateral to ulnar nerve.</p> <p>BRANCHES :</p> <ul style="list-style-type: none"> • Muscular branches • Common interosseous artery: Arises from the upper part of Ulnar artery and divides into anterior and posterior branches. • Palmar branch: joins radial artery to complete deep palmar arch
Scapular Anastomosis	<p>It occurs at 2 sites:</p> <p>around the body of the scapula and over acromion process of the scapula.</p> <p>Created between the branches of the first Part of the subclavian and the third part of the axillary arteries.</p> <ol style="list-style-type: none"> 1. Around the body of the scapula: It takes place between the: <ul style="list-style-type: none"> • Suprascapular artery, a branch of the thyrocervical trunk from the 1st part of the Subclavian artery

	<ul style="list-style-type: none"> • Circumflex scapular artery, a branch of the subscapular artery from the third part of the Axillary artery • Dorsal scapular artery frequently arises from the subclavian artery (the second or third part). It is the direct branch of subclavian artery that takes part in shoulder anastomosis. <p>2. Over the acromion process: It takes place between the Acromial branches of :</p> <ul style="list-style-type: none"> ○ Thoraco-acromial artery ○ Suprascapular artery ○ posterior circumflex humeral artery. 	
Palmar arches	<p>Deep palmar arch (deep volar arch) :</p> <ul style="list-style-type: none"> ○ An arterial network in palm ○ Primarily formed from the terminal part of the radial artery. The ulnar artery also contributes through an anastomosis. 	<p>Superficial palmar arch:</p> <ul style="list-style-type: none"> ○ formed predominantly by Ulnar artery.
VENOUS DRAINAGE		
<p>1. Superficial venous system: Basilic, cephalic, median cubital – they are not accompanied by arteries</p> <p>2. Deep venous system: paired veins accompanying the arteries, lie under deep fascia.</p> <ul style="list-style-type: none"> ○ Dorsal venous arch divides into Cephalic vein (lateral) and Basilic vein (medial) ○ From cephalic vein → Median cubital vein arises which drains into Basilic vein. 		
Cephalic vein	Basilic vein	Median cubital vein
<ul style="list-style-type: none"> • Arise from the lateral side of the dorsal venous arch, begins in an anatomic snuff box. • Ascends on the radial side of the forearm to elbow. • Pierces deltopectoral fascia and drain into Axillary vein in clavipectoral triangle. • It is likely to bleed due to sharp cut at anatomical snuff box. • The cephalic vein is favoured vessels for arteriovenous fistula formation and should be Preserved in a patient with end-stage renal failure 	<ul style="list-style-type: none"> • Arise from the medial side of the dorsal venous arch and Ascend on the ulnar side of the forearm to the elbow. 	<p>Links cephalic and Basilic vein in the cubital fossa.</p> <ul style="list-style-type: none"> • Used for venesection.
<p>Deep Venous system</p> <ul style="list-style-type: none"> • Underlies deep fascia, consists of paired vein, accompany the artery, and have same name as the artery. • Brachial veins -- the largest one among them. The pulsation of brachial artery assists venous return. • The veins that are structured in this way are called vena comitans (accompanying veins) • Axillary vein formed by Basilic vein and vena comitantes of brachial artery at the lower border of teres major muscle. • Perforating veins: run b/w superficial and deep vein and connect them. 		





UPPER LIMB LYMPHATICS



Mnemonic for axillary lymph nodes:
"APICAL"

A - Anterior
P - Posterior
I - Infraclavicular
C - Central
A - Apical
L - Lateral

75% of lymphatics from the breast drain to axillary nodes. Others to internal thoracic, abdominal nodes or to other breast

LYMPHATIC DRAINAGE

Lymphatics from the upper limb drain into lymph nodes in the Axillary node.

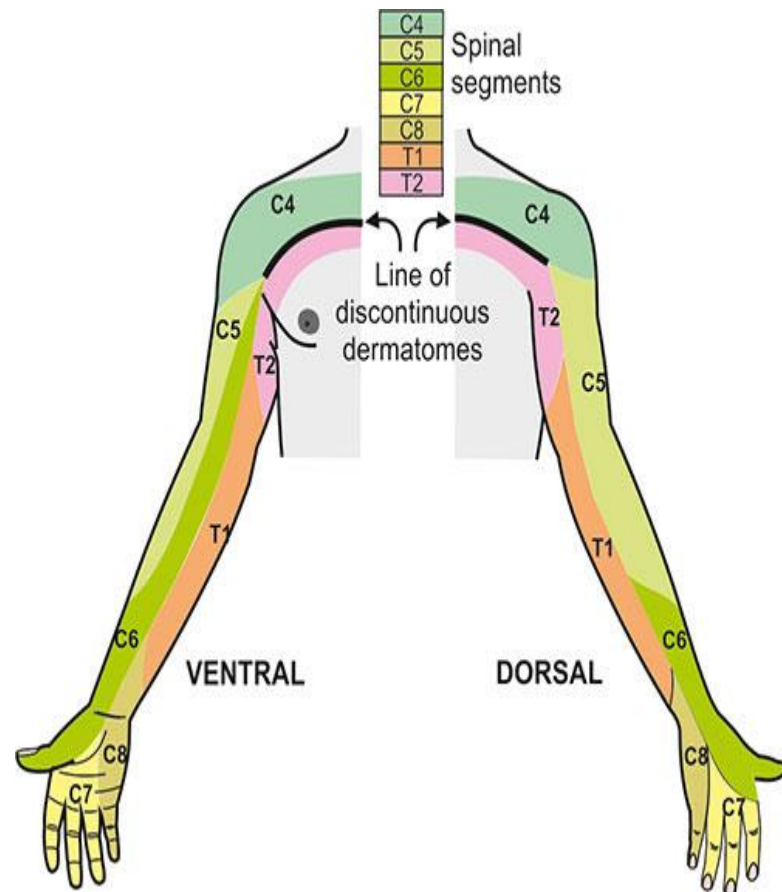
The 20-30 axillary nodes are generally divided into groups based on location.

Humeral/Lateral nodes	<ul style="list-style-type: none"> ○ Posteromedial to the Axillary vein. ○ Receive most of the lymph from the upper limb. ○ Supratrochlear lymph node drains the Middle, ring and little finger, the medial portion of the hand and the medial side of the forearm. ○ The efferent enter lateral axillary nodes
Pectoral/Anterior nodes	<ul style="list-style-type: none"> ○ Present along the inferior margin of the pectoralis minor muscle Along the course of the lateral thoracic vessels. ○ Receive drainage from the abdominal wall, chest, and mammary gland.
Subscapular/Posterior nodes	<ul style="list-style-type: none"> ○ Lie on the posterior Axillary wall in association with the Subscapular vessels. ○ Drain the posterior Axillary wall and receive lymphatics from the back, shoulder, and the neck.
Central nodes	<ul style="list-style-type: none"> ○ They are embedded in axillary fat. ○ They receive tributaries from Humeral, Subscapular, and, Pectoral groups
Apical nodes	<ul style="list-style-type: none"> ○ Are the most superior group of nodes in the axilla and drain all other groups of nodes in the region. ○ In addition, they receive lymphatic vessels that accompany the cephalic Vein as well as vessels that drain the superior region of the mammary gland.
Infraclavicular nodes	<ul style="list-style-type: none"> ○ They drain lymph from thumb Consisting of its web and upper part of the breast.
Efferents	
<ul style="list-style-type: none"> ○ Efferent vessels from the apical group converge to form the subclavian trunk, which usually joins the venous system at the junction between the right subclavian vein and the right internal jugular Vein in the neck. ○ On the left, the subclavian trunk usually joins the thoracic duct in the base of the Neck. 	
Significance	
<ul style="list-style-type: none"> ○ Lymphatic drainage from the lateral part of the breast passes through nodes in the axilla. ○ Significant disruption to the normal lymphatic drainage of the upper limb may occur if a Mastectomy or a surgical axillary nodal clearance has been carried out for breast cancer. ○ If the lymph drainage is damaged, the arm may swell, and pitting Edema (lymphedema) may develop. 	

DERMATOMES & MYOTOMES

Upper limbs are innervated by spinal nerves C5-T2.

○ C1: No skin	○ Supraclavicular : C2 , C3	○ C6 -shoulders and longitudinally down the middle posterior aspect of the upper limb, radial side of the hand, thumb
○ C2 – occipital region	○ Infraclavicular: C3, C4	○ C7-hand, middle finger
○ C3: Neck	○ Clavicles- C5	○ C8-ulnar side of the hand , ring finger, and little finger
○ It can be transacted to relieve severe shooting neck pain	○ anterior skin below the clavicles spreading over the lateral aspect of the upper limb, posterior Skin around the base of the neck	
❖ T1-level of the infraclavicular fossa, extending to the medial aspect of the forearm.		
❖ T2 – anterior and posteriorly extends at the level of the upper axilla and medial and upper aspect of arm		
❖ Infraclavicular region (to manubriosternal junction)-C4		
❖ C6 Bicep jerk		
❖ C7 Triceps jerk (lower cervical segment)		
❖ Lateral side of upper limb → C5, C6		
❖ Medial side of upper limb → C8, T1		
❖ Level of nipples—T4		



Carpal Tunnel Syndrome

- **Risk factors:** Obesity, females, pregnancy, myxoedema, genetic predisposition
- Sensory loss > Motor Loss
- Pain & Paraesthesia in lateral 3 ½ digits > Thenar Wasting / loss of thumb opposition
- Wrist flexion produces symptoms: called Phalen's test
- Tapping over Median nerve causes tingling: Tinel's test
- Night pain is common that is relived upon shaking hand.

Bicipital Groove of Humerus - Attached Muscles:

Lady between Two Major

1. **Teres Major** Attach on the medial side of the bicipital groove
 2. **Pectoralis Major** Attach on the lateral side of the bicipital groove
 3. **Latissimus dorsi** inserted in the floor of the bicipital groove.
- All these three muscles cause Adduction and Medial rotation

Serratus Anterior Muscle

- Long Thoracic nerve- C5,6,7 supplies SA.
- **boxer, punching and pushing muscle** and tested by asking patient to push against the wall.
- Commonly injured during radical mastectomy caused winged scapula and ipsilateral Lymphedema.

Latissimus Dorsi Muscle

- Thoracodorsal nerve supply. Causes downward displacement of glenohumeral ligaments.
- extends the shoulder joint and medially rotates the humerus e.g., folding the arms Behind the back or scratching the opposite scapula
- **Swimming / Climbing Muscle.**
- Injury: Patient will be unable to scratch back (dorsum)

Pectoralis Muscles

- **Pect Major flexes**, adducts and medially rotates the arm, supplied by Medial & lateral pectoral nerves
- Pect Major may be absent congenitally
- **Pect Minor** helps Rhomboids in protraction and depression of scapula. Supplied by Med pectoral nerves.
- **Medial Epicondylitis** / Golfer & Baseball's elbow: involves inflammation of Common Flexor tendons
- **Lateral Epicondylitis** / Tennis Elbow: Inflamed common Extensor tendon.
- Brachialis & Flexor digitorum Profundus have Hybrid nerve supply.

BREAST

- A Modified sebaceous gland
- Extends Vertically: 2nd-6th rib, horizontally: lateral border of sternum to mid axillary line.
- **Breast lies over Superficial Pectoral fascia & Pectoralis major.**
- Breast is separated from pectoral fascia by loose areolar tissue known as Retro mammary space and Breast can move freely over pectoralis major due to this space.
- Nipple is Conical projection at the level of 4th intercostal space. Pierced by 15-20 lactiferous ducts.
- **Parenchyma:** Glandular tissue secretes milk.
- Consists of 15 to 20 lobes. **Each lobe is cluster of alveoli and is drained by lactiferous ducts.**
- Lactiferous ducts pierce the nipple (lactiferous sinus- → ampulla)
- **Stroma:** Forms the supporting framework of gland. Partly fibrous and partly fatty.
- Fibrous stroma: forms septa known as suspensory ligaments of Cooper.
- Fatty stroma forms the main bulk of the gland. Difference b/w male and female breast is of glandular tissue.

Neurovascular Supply

- Internal thoracic artery (branch of subclavian artery)
- Lateral thoracic artery (branch of axillary artery), Intercostal arteries
- Internal thoracic vein, axillary vein
- **Nerves:** 4th to 6th intercostal nerve. Nerves do not control the secretion of milk.
- Secretions are controlled by prolactin.

Lymphatic Drainage

- Axillary lymph nodes (PECTORAL Nodes mainly)
- Others: Internal mammary nodes. Subdiaphragmatic and sub peritoneal lymph plexuses

Quadrants of Breasts

Medial and Lateral 4 quadrants:

1. Superolateral (Upper Outer) → 70 % of cancers of breast involve Upper Outer/Superolateral group.
2. Superomedial (Upper Inner)
3. Inferolateral (Lower Outer)
4. Inferomedial (lower inner)

Pathway of Axillary Lymph drainage: Anterior and Posterior Nodes

- **75% of Lymph of breast drains into Anterior group (Pectoral grp).**
- Upper Lateral drains into Anterior Axillary/Pectoral mainly
- Lower lateral into Ant axillary, Subdiaphragmatic & internal mammary nodes
- Medial Quadrant drains into internal mammary / internal thoracic nodes.
- Inferomedial quadrant drains into Subdiaphragmatic/inferior phrenic nodes.
- Nipple drains into Ant Axillary nodes.
- Tail of breast drains into Posterior Axillary/Scapular Nodes.

Significance:

- Sentinel lymph node is the 1st node in which cancer drains.
- Biopsy of sentinel node helps in establishing prognosis of carcinoma.
- **Axillary lymph node biopsy helps in assessing: Bilateral disease > prognosis regarding breast carcinoma.**

PAST PAPERS BCQs

1. All small muscles of Hand wasting without lateral sparing: C8+T1 Lesion
2. All small muscles of Hand wasting with lateral sparing = Ulnar nerve lesion
3. Loss of flexion + Supination = Musculocutaneous nerve lesion
4. Loss of extension + Supination = Radial nerve injury
5. Suprascapular + Thoraco acromial arteries supply Acromioclavicular joint.
6. No sensory Loss, Loss of MCP Flexion, Loss of Thumb abduction = Posterior interosseous > Radial nerve injury
7. Teres minor = lateral rotation +adduction+ extension. axillary nerve supplies it.
8. Teres Major = Medial rotation + Adduction. Supplied by Lower subscapular nerve.
9. Rhomboids are supplied by Dorsal scapular nerve.
10. Supracondylar fracture causes = Median nerve + brachial artery injury.
11. Abd Pollicis Longus supplied by Radial nerve; Abd Pollicis Brevis by: Median nerve.
12. Pect minor attaches at = Coracoid process of scapula
13. Radial pulse is palpated b/w = Abductor Pollicis Longus & Extensor Pollicis Longus
14. Unable to adduct & abduct fingers = Ulnar nerve lesion
15. Supraspinatus is mostly damaged in = Rotator cuff damage
16. In Supinator damage Biceps brachii performs = supination
17. Lumbricals are = flexors of MCP Joints
18. In Posterior dislocation of elbow = Ulnar collateral ligament is damaged.
19. C5/C6 roots are damaged, affect = infraspinatus muscle affected.
20. Can't grip the card b/w thumb & index finger = Anterior interosseous Nerve lesion
21. Can't Pinch the paper b/w thumb & index finger = Fromet's sign—Ulnar nerve lesion
22. Pect minor lies Infront of = 2nd part of axillary artery
23. Palmaris brevis is only muscle supplied by = Superficial branch of Ulnar nerve
24. T7 = inferior angle of scapula
25. Pt in abducted hand is asked to move hand slowly downward but he dropped hand suddenly =supraspinatus damage
26. Axillar Vein formed by = Basilic vein & Vena comitans of brachial artery
27. Axillary nerve helps in = lateral rotation of arm
28. Levator scapulae supply = C4, C5
29. C8 Present in = Posterior Cord
30. Extensor carpii Ulnaris supply = Post interosseous nerve
31. Medial attachment of flexor retinaculum = Pisiform bone
32. Triceps reflex loss lesion in = Lower cervical segments (C6, C7)
33. Abd digiti minimi is NOT affected in = carpal tunnel syndrome
34. Numbness of Root / Base of thumb = Radial nerve lesion
35. Medial epicondyle fracture = Ulnar nerve + Ulnar collateral artery damaged.
36. In Quadrangular space injury = Axillary nerve & Post Circumflex artery is damaged (same in ant disloc of shoulder)
37. Medial epicondyle is common flexor origin
38. C2,3 → Greater Auricular Nerve. C3,4 → Supraclavicular nerve. C3,4,5 → Phrenic Nerve
39. C5,6 → Axillary nerve; C5-6-7 → Musculocutaneous Nerve and Long thoracic nerve.
40. C6-7-8 → Thoracodorsal Nerve
41. C5 – T1 → Median and Radial Nerve; C8-T1 → Ulnar nerve
42. During radical mastectomy the nerve to serratus anterior and nerve to latissimus dorsi is preserved
43. Parts of clavipectoral fascia lies deep to pec major and its fascia. It is pierced by = cephalic vein, lateral pectoral nerve, Thoracoacromial vessels, lymphatics.
44. Radial nerve = largest branch of brachial plexus
45. Subacromial bursitis, supraspinatus tendinitis and peri capsulitis of shoulder joint causes very painful movement in middle range of abduction b/w 50 to 130 degree. This is called = painful arc
46. Most important ligament for suspending upper limb from clavicle and scapula is = coracoclavicular ligament
47. Up to 120-degree abduction of arm at shoulder joint: for every 3 degrees of abduction of arm, 2 degree occurs in shoulder joint and 1 degree by rotating the scapula. After 120 degrees only scapula rotates

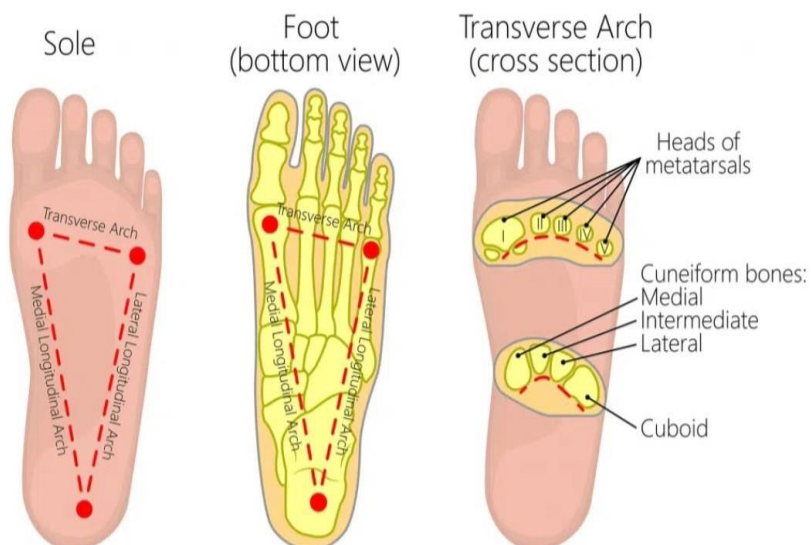
48. Median nerve has no branches in upper arm except that of vasomotor branches to brachial artery
49. Ulnar nerve has no branch in anterior compartment of upper arm
50. Bones of hand are cartilaginous at the time of birth. First bone of the hand to be ossified is capitate
51. Compartment syndrome: early signs and symptoms are altered sensations, pain disproportionate to injury, pain by passive stretching of muscles. Late signs and symptoms are tenderness and failure of capillary refilling.
52. Volar carpal ligament: a superficial slip of flexor retinaculum is attached to pisiform bone. Called volar carpal ligament. Ulnar artery and nerve pass deep to it.
53. Superficial branch of radial nerve = is direct continuation of radial nerve
54. Rupture of extensor pollicis longus tendon occurs after fracture of distal third of radius
55. Space of parona is the space b/w flexor digitorum Profundus anteriorly and pronatus quadrates and interosseous membrane posteriorly.
56. In case of infection of digital sheath of little finger and thumb the pus may burst thru proximal ends of ulnar and radial bursa and enter this space.
57. Blood supply of epiphysis of distal phalanx of fingers is outside the pulp space. While that of diaphysis is inside the pulp space. infection causing increased pressure can cause necrosis of diaphysis and epiphysis is spared
58. Nerve affected by cubital tunnel syndrome: Ulnar Nerve compressed
59. carpal tunnel syndrome: Median Nerve
60. Region affected by lower trunk injury of brachial plexus (C8-T1) = Intrinsic hand muscles
61. Innervations to all interosseous muscles =Ulnar (deep branch) & innervation of adductor Pollicis: Ulnar (deep branch)
62. Nerve to thenar compartment = recurrent Branch of Median
63. Dermatome of thumb: C6 & Spinal levels of innervations to muscles of the hand: C8 and T1
64. Primary (major) flexor of the forearm: Brachialis
65. Chief supinator muscle: biceps brachii
66. A tendon that courses through shoulder joint: long head of biceps
67. Two muscles that rotate scapula for full abduction of arm: trapezius and serratus anterior.
68. Most frequently fractured bone of body: clavicle.
69. Most frequently dislocated carpal bone: lunate
70. Most frequently fractured carpal bone: scaphoid
71. Osseous structure palpated deep to "anatomical snuff box" scaphoid.
72. Fracture of distal radius that produces "dinner fork" Appearance: Colles's fracture.
73. Nerve injured with fracture of shaft of humerus: Radial nerve.
74. Nerve injured with fracture of surgical neck of humerus: axillary.
75. Nerve injured with fracture of medial humeral epicondyle: ulnar.
76. Muscle that is the chief flexor and chief extensor at shoulder joint: Deltoid
77. Muscles innervated by axillary nerve: Deltoid and teres minor.
78. Muscle that initiates abduction of arm: supraspinatus
79. Most torn tendon of rotator cuff: supraspinatus.
80. Overhead abduction: Only Serratus anterior

LOWER LIMB

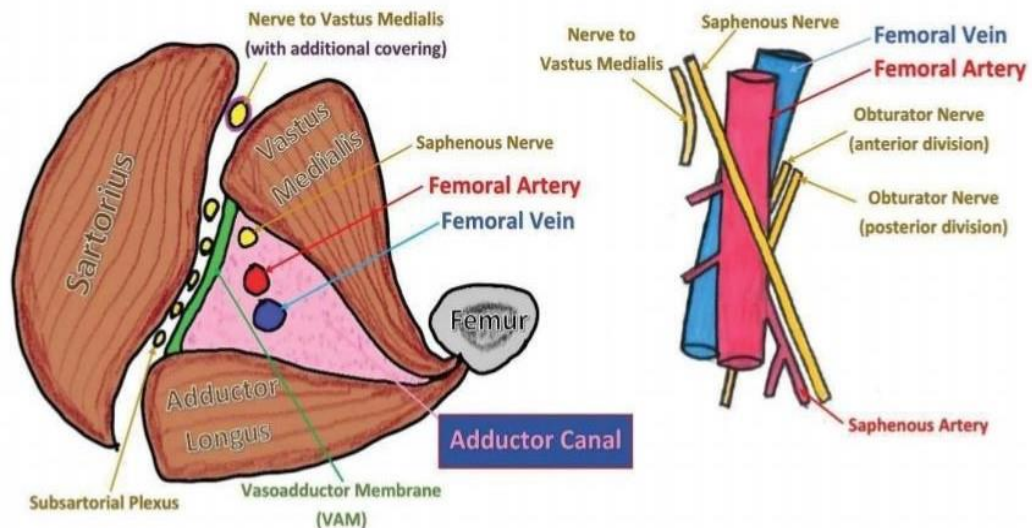
BONES	
Hip Bone	<ul style="list-style-type: none"> Irregular bone, made of Ilium (largest), ischium & Pubis. Ischiopubic rami fuse at 07 yrs. of age Transtubercular plane L4/L5: passes through iliac tubercles – the highest point of Iliac Crests. Floor of acetabulum: formed by Ilium + Ischium > ischium + Pubis. Iliofemoral Ligament prevents over extension of Hip joint – strongest ligament of body. We sit on the ischial tuberosities → (give attachment to Hamstrings muscles) For bone marrow biopsy, Prefer. <p>Ventral iliac crest > Posterior Iliac crest > Vertebrae > Tibia > Sternum</p>
Femur	<ul style="list-style-type: none"> Largest long bone of body, avascular necrosis of neck occurs in elderly pts. Neck is Prone to fracture by trivial trauma due to osteoporotic bone in old age. Fracture of neck may result in Limb shortening & leg in abducted position. Bloods supply of Neck: Medial & Lateral Circumflex arteries Blood supply of Head: Retinacular arteries > Medial Circumflex in adults Obturator arteries supply in Child. Avascular necrosis: Retinacular artery > Medial circumflex femoral. (Mostly option of Medial Circumflex given) Medial lip of Linea aspersa continues as Pectineal /Spiral line which further continues as Inter-Trochanteric line. Lateral lip of Linea aspersa joins: Gluteal tuberosity. Femur is 2nd common fractured bone in lower limb after tibia in adults. It is the MC fractured bone in old age. On posterior surface of shaft: Gluteal tuberosity is present below greater trochanter to give insertion to Glut Maximus The neck of the femur is inclined at an angle of about 160° in the young child and 125° in the adult with the shaft. increase in the angle is Coxa valga. A decrease in angle is referred to as Coxa Vara
Tibia	<ul style="list-style-type: none"> Most fractured lower limb long bone in adults due to RTA Located Medially in leg. Stress fracture of shaft occurs in military recruits / runners. For bone marrow biopsy in <1 yr. infants, medial side of Upper Tibia can be used.
Fibula	<ul style="list-style-type: none"> Laterally located, graft is taken from middle shaft of fibula Fibula violates/doesn't obey the law of Ossification. Doesn't take part in knee joint formation but forms ankle joint
Patella	<ul style="list-style-type: none"> Largest sesamoid bone, present in the tendon of Quadriceps femoris. The most dislocated bone in the body.
Foot	<ul style="list-style-type: none"> 3 groups of bones in the foot the seven tarsal bones, Metatarsals (I to V) & phalanges. Tarsal bones = Calcaneum, Talus, Navicular, Cuboid, Cuneiform -3 The tarsal bones are arranged in a proximal group and a distal group with an intermediate bone B/w them. <ol style="list-style-type: none"> Proximal group: consists of two large bones, the talus and the calcaneum bone. No muscular attachment at talus bone and, it forms the pillar of the medial arch. Calcaneus: largest of the tarsal bones-posteriorly it forms bony framework of the heel Intermediate tarsal bone: on the medial side of the foot is the navicular (boat shaped) One distinctive feature of the navicular is a prominent rounded tuberosity for the attachment of the tibialis posterior tendon. Distal group: From lateral to medial The cuboid (Greek for cube), which articulates behind with calcaneus. Three cuneiforms Articulate behind with navicular bone and in front with the bases Metatarsals.

JOINTS											
Hip joint	<p>Synovial ball and socket joint formed b/w Head of Femur & Acetabulum It is mostly dislocated posteriorly.</p> <ul style="list-style-type: none"> Femoral nerves & Vessels pass anteriorly while Sciatic nerve passes posteriorly. <table> <tr> <td>Ligaments</td><td> <ul style="list-style-type: none"> iliofemoral ligament - Strongest ligament and most important ligament of hip joint, Y shaped Prevent hyperextension and lateral rotation. Ischiofemoral ligament: Spiral shape, Weakest. Prevent medial rotation. Pubofemoral ligament: Triangular, Prevents extensive abduction and lateral rotation Ligament of Head of Femur: Ligamentum teres / Round Ligament Acetabulum Labrum Transverse Ligament of acetabulum </td></tr> <tr> <td>Movements</td><td> <ul style="list-style-type: none"> Flexion - Psoas major, Sartorius, Iliacus & Rectus femoris Extension - Gluteus maximum > Hamstrings Abduction -- Glut. Med & minimus, Sartorius, tensor fascia lata, Adduction -- Adductor longus, Magnus & brevis Medial Rotation — Glut Medius & Minimus Lateral Rotation — Glut max, gemelli, Piriformis </td></tr> </table>	Ligaments	<ul style="list-style-type: none"> iliofemoral ligament - Strongest ligament and most important ligament of hip joint, Y shaped Prevent hyperextension and lateral rotation. Ischiofemoral ligament: Spiral shape, Weakest. Prevent medial rotation. Pubofemoral ligament: Triangular, Prevents extensive abduction and lateral rotation Ligament of Head of Femur: Ligamentum teres / Round Ligament Acetabulum Labrum Transverse Ligament of acetabulum 	Movements	<ul style="list-style-type: none"> Flexion - Psoas major, Sartorius, Iliacus & Rectus femoris Extension - Gluteus maximum > Hamstrings Abduction -- Glut. Med & minimus, Sartorius, tensor fascia lata, Adduction -- Adductor longus, Magnus & brevis Medial Rotation — Glut Medius & Minimus Lateral Rotation — Glut max, gemelli, Piriformis 						
Ligaments	<ul style="list-style-type: none"> iliofemoral ligament - Strongest ligament and most important ligament of hip joint, Y shaped Prevent hyperextension and lateral rotation. Ischiofemoral ligament: Spiral shape, Weakest. Prevent medial rotation. Pubofemoral ligament: Triangular, Prevents extensive abduction and lateral rotation Ligament of Head of Femur: Ligamentum teres / Round Ligament Acetabulum Labrum Transverse Ligament of acetabulum 										
Movements	<ul style="list-style-type: none"> Flexion - Psoas major, Sartorius, Iliacus & Rectus femoris Extension - Gluteus maximum > Hamstrings Abduction -- Glut. Med & minimus, Sartorius, tensor fascia lata, Adduction -- Adductor longus, Magnus & brevis Medial Rotation — Glut Medius & Minimus Lateral Rotation — Glut max, gemelli, Piriformis 										
Knee joint	<ul style="list-style-type: none"> A compound, complicated hinge joint formed b/w femur, tibia, and patella. Femoral, Sciatic and obturator nerve supply it. Intracapsular ligaments: ACL, PCL, and Menisci (fibrocartilage) Extracapsular Ligaments: Medial and Lateral Collateral Ligament, Oblique Popliteal Ligament, and Ligamentum patellae. <ol style="list-style-type: none"> Anterior cruciate ligament (ACL) → Most common knee ligament injured. It prevents Anterior dislocation of TIBIA on femur and Posterior dislocation of Femur on tibia. Positive anterior drawer sign --- ACL tear Posterior cruciate ligament → Prevents Anterior dislocation of Femur on tibia while Posterior dislocation of Tibia on femur. Ligamentum patellae → It is the condition of the tendon of quadriceps femoris. Oblique Popliteal ligament → Tendinous expansion of semimembranosus muscle. It strengthens the posterior Aspect of the capsule. Medial collateral ligament (MCL) → Medial stabilizer of the knee and is most injured by direct blow to the lateral aspect (outside) of the knee or by the patient planting the foot and then colliding with another athlete. Lateral collateral ligament (LCL) → Injury occurs via hyperextension with varus stress or from a direct blow or rotation. LCL Damaged by blow to medial side- inside (Varus force) <table> <tr> <td>Movements</td><td> <ul style="list-style-type: none"> Flexion - Biceps femoris, Semi tendinosis, semi membranous, and, gracillus. Extension- Quadriceps femoris Medial Rotation--- Semi tendinosis, semi membranous Lateral Rotation-- Biceps femoris </td></tr> <tr> <td>Locking vs unlocking</td><td> <ul style="list-style-type: none"> Quadriceps Femoris: Locking of knee. Popliteus: Unlocks the knee by laterally rotating femur </td></tr> <tr> <td>Stability</td><td> <ul style="list-style-type: none"> Stability of Knee: Vastus Lateralis Stability of Patella: Vastus Medialis </td></tr> <tr> <td>Unhappy triad</td><td> <ul style="list-style-type: none"> Also called Blow knee → ACL, MCL, Medial menisci are called the unhappy triad, because they are commonly injured </td></tr> <tr> <td>Housemaid knee</td><td> <ul style="list-style-type: none"> Prepatellar bursitis/housemaid's knee caused by inflammation of prepatellar bursa in individuals who spend long periods kneeling, such as housemaids, clergy, and gardeners </td></tr> </table>	Movements	<ul style="list-style-type: none"> Flexion - Biceps femoris, Semi tendinosis, semi membranous, and, gracillus. Extension- Quadriceps femoris Medial Rotation--- Semi tendinosis, semi membranous Lateral Rotation-- Biceps femoris 	Locking vs unlocking	<ul style="list-style-type: none"> Quadriceps Femoris: Locking of knee. Popliteus: Unlocks the knee by laterally rotating femur 	Stability	<ul style="list-style-type: none"> Stability of Knee: Vastus Lateralis Stability of Patella: Vastus Medialis 	Unhappy triad	<ul style="list-style-type: none"> Also called Blow knee → ACL, MCL, Medial menisci are called the unhappy triad, because they are commonly injured 	Housemaid knee	<ul style="list-style-type: none"> Prepatellar bursitis/housemaid's knee caused by inflammation of prepatellar bursa in individuals who spend long periods kneeling, such as housemaids, clergy, and gardeners
Movements	<ul style="list-style-type: none"> Flexion - Biceps femoris, Semi tendinosis, semi membranous, and, gracillus. Extension- Quadriceps femoris Medial Rotation--- Semi tendinosis, semi membranous Lateral Rotation-- Biceps femoris 										
Locking vs unlocking	<ul style="list-style-type: none"> Quadriceps Femoris: Locking of knee. Popliteus: Unlocks the knee by laterally rotating femur 										
Stability	<ul style="list-style-type: none"> Stability of Knee: Vastus Lateralis Stability of Patella: Vastus Medialis 										
Unhappy triad	<ul style="list-style-type: none"> Also called Blow knee → ACL, MCL, Medial menisci are called the unhappy triad, because they are commonly injured 										
Housemaid knee	<ul style="list-style-type: none"> Prepatellar bursitis/housemaid's knee caused by inflammation of prepatellar bursa in individuals who spend long periods kneeling, such as housemaids, clergy, and gardeners 										

<p>Ankle joint</p>	<p>It is synovial in type and involves the talus of the foot and the tibia and fibula of the Leg. Allows hinge-like dorsiflexion and Plantarflexion of the foot.</p> <table border="1"> <tr> <td data-bbox="352 257 566 705"> <p>Ligaments</p> </td><td data-bbox="566 257 1532 705"> <ol style="list-style-type: none"> Deltoid ligament/Medial Lig is large, strong, and triangular. Injury occurs due to Excessive Eversion of foot. Lateral ligament → Weaker than medial ligament and consist of three bands. <ol style="list-style-type: none"> Anterior talofibular ligament Posterior talofibular ligament Calcaneofibular ligament <ul style="list-style-type: none"> Most common type of injury is inversion because of this weak lateral ligament. Most common ligament injury is lateral ligament and most common among subtype Ligament injury is of anterior talofibular ligament Twisting inversion accounts for the common strain to anterior talofibular part of Lateral ligament </td></tr> <tr> <td data-bbox="352 705 566 806"> <p>Movements</p> </td><td data-bbox="566 705 1532 806"> <p>Dorsiflexion: Tibialis anterior, PERONEUS tertius Planter flexion: Peroneus longus, Peroneus Brevis, plantaris, soleus, Gastrocnemius</p> </td></tr> <tr> <td data-bbox="352 806 566 884"> <p>Key fact</p> </td><td data-bbox="566 806 1532 884"> <p>In Plantaris tendon rupture: Patient can stand on foot but painful. Achilles tendon rupture: Patient can't stand on the toes</p> </td></tr> </table>	<p>Ligaments</p>	<ol style="list-style-type: none"> Deltoid ligament/Medial Lig is large, strong, and triangular. Injury occurs due to Excessive Eversion of foot. Lateral ligament → Weaker than medial ligament and consist of three bands. <ol style="list-style-type: none"> Anterior talofibular ligament Posterior talofibular ligament Calcaneofibular ligament <ul style="list-style-type: none"> Most common type of injury is inversion because of this weak lateral ligament. Most common ligament injury is lateral ligament and most common among subtype Ligament injury is of anterior talofibular ligament Twisting inversion accounts for the common strain to anterior talofibular part of Lateral ligament 	<p>Movements</p>	<p>Dorsiflexion: Tibialis anterior, PERONEUS tertius Planter flexion: Peroneus longus, Peroneus Brevis, plantaris, soleus, Gastrocnemius</p>	<p>Key fact</p>	<p>In Plantaris tendon rupture: Patient can stand on foot but painful. Achilles tendon rupture: Patient can't stand on the toes</p>
<p>Ligaments</p>	<ol style="list-style-type: none"> Deltoid ligament/Medial Lig is large, strong, and triangular. Injury occurs due to Excessive Eversion of foot. Lateral ligament → Weaker than medial ligament and consist of three bands. <ol style="list-style-type: none"> Anterior talofibular ligament Posterior talofibular ligament Calcaneofibular ligament <ul style="list-style-type: none"> Most common type of injury is inversion because of this weak lateral ligament. Most common ligament injury is lateral ligament and most common among subtype Ligament injury is of anterior talofibular ligament Twisting inversion accounts for the common strain to anterior talofibular part of Lateral ligament 						
<p>Movements</p>	<p>Dorsiflexion: Tibialis anterior, PERONEUS tertius Planter flexion: Peroneus longus, Peroneus Brevis, plantaris, soleus, Gastrocnemius</p>						
<p>Key fact</p>	<p>In Plantaris tendon rupture: Patient can stand on foot but painful. Achilles tendon rupture: Patient can't stand on the toes</p>						
<p>Subtalar joint</p>	<p>Inversion and Eversion occurs at Subtalar joint.</p> <ul style="list-style-type: none"> Inversion → Tibialis anterior and Tibialis posterior, extensor hallucis longus, and, extensor digitorum longus (medial fibers). Eversion: pEroneus longus, brevis and tertius, Extensor digitorum longus (lateral fibres). 						
<p>ARCHES OF FOOT</p>							
<p>Medial</p>	<ul style="list-style-type: none"> ✓ Pillar of medial arch is formed by talus bone. ✓ Med arch Formed by all tarsal bone except- cuboid bone and lateral tarsal bone. ✓ Most important ligament in medial arch – plantar calcaneonavicular ligament ✓ KEY BONE or stone: TALUS, also anteriorly imp. ✓ Posteriorly: arch formed by: Calcaneum 						
<p>Lateral</p>	<ul style="list-style-type: none"> ✓ Formed by cuboid bone, lateral two metatarsal and calcaneum. ✓ KEY BONE: CUBOID. Peroneus longus and brevis suspend the arch from above 						
<p>Transverse</p>	<ul style="list-style-type: none"> ✓ Formed by cuboid bone, three cuneiform bones and bases of metatarsal bones. ✓ Fall from height may damage transverse / anterior arch. 						



Gluteal Muscles	<ul style="list-style-type: none"> ▪ The gluteus Maximus, gluteus Medius and gluteus Minimus: ▪ The three muscles originate from ilium and sacrum and insert on the femur. ▪ GLUT MAX: An extensor Muscle responsible for prominence of buttock, supplied by inferior gluteal nerve—L5, S1, S2 ▪ Inferior gluteal nerve may be injured in Posterior Hip Dislocation. ▪ IM injection in Gluteus Maximus in upper lateral Quadrant to avoid damage to: Sciatic nerve > Superior Gluteal nerve (SGN) ▪ Glut max is Anti-Gravity muscle, helps in standing from sitting position and jumping up Or Climbing stairs. ▪ Glut Med & Minimus are supplied by Superior gluteal nerve (SGN) ▪ SGN: Nerve Lesion may occur in Posterior Hip dislocation, stab wound or Polio. ▪ Trendelenburg's Sign/Waddling Gait - To test the weak abductors i.e., gluteus med & Minimus. <p>✓ in injury of Superior gluteal nerve. (L4, L5, S1), Ask the patient to stand on one leg, pelvis sinks on the contralateral side when standing on affected leg.</p> <p>✓ If pelvis sags to right, it means that the left side is damaged.</p>
COMPARTMENTS OF THIGH	
Anterior	<ul style="list-style-type: none"> ▪ Muscle which flexes the thigh and extend the leg is rectus femoris that originates from Ant- inf Iliac spine. ▪ All ant compartment muscles supplied by femoral nerve except psoas which is supplied by lumbar plexus ▪ Sartorius muscle: Flexor of both hip and knee joint -- Originates from anterior superior iliac spine and insert on proximal tibia, medial to tibial tuberosity ▪ Fracture of anterior superior iliac spine will cause damage to Sartorius. ▪ Four large quadriceps femoris muscles (rectus femoris, vastus lateralis, vastus medialis, And vastus intermedius) ▪ The rectus femoris muscle crosses both the hip and the knee joints. Vastus lateralis originates from the femur and contribute directly to the stability of the Knee joint. ▪ Iliacus muscle ▪ Psoas muscle Supplied by lumbar plexus, Forms medial Arcuate ligament. Originates from all lumbar vertebrae
Medial	<ul style="list-style-type: none"> ▪ Contains hip adductors: Obturator externus, Adductor brevis Adductor longus and Adductor Magnus: ▪ All are Supplied by Obturator nerve. (pain is referred to the medial of thigh in ovarian cancer through obturator nerve) ▪ Adductor Magnus is the largest and deepest of the muscles in the medial Compartment of thigh. It has two parts: <ul style="list-style-type: none"> ○ Adductor portion---supplied by Obturator nerve. ○ Hamstring portion—supplied by tibial nerve
Posterior	<ul style="list-style-type: none"> ○ contains three large muscles termed the 'hamstrings' Muscles ○ Biceps femoris: two heads: ○ Short head supplied by sciatic nerve; Longhead supplied by tibial nerve ○ 2- semitendinosus. 3- Semimembranosus
ADDUCTOR CANAL (Hunter canal)	
Boundaries	<ul style="list-style-type: none"> ○ Anteromedial: Sartorius ○ Lateral: vastus medialis ○ Posterior: Adductor longus and adductor Magnus.
Contents	<ul style="list-style-type: none"> ○ Terminal part of femoral artery and vein ○ Terminal part of Obturator nerve, Saphenous nerve, and nerve to vastus medialis.

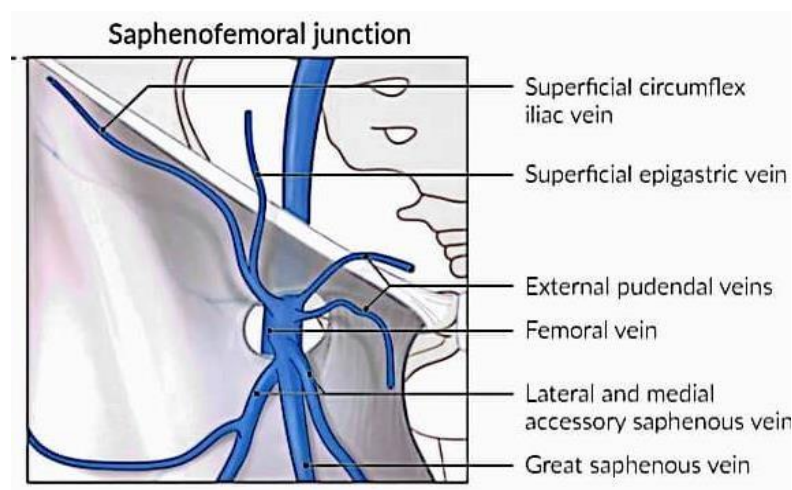


SEPHENOUS OPENING

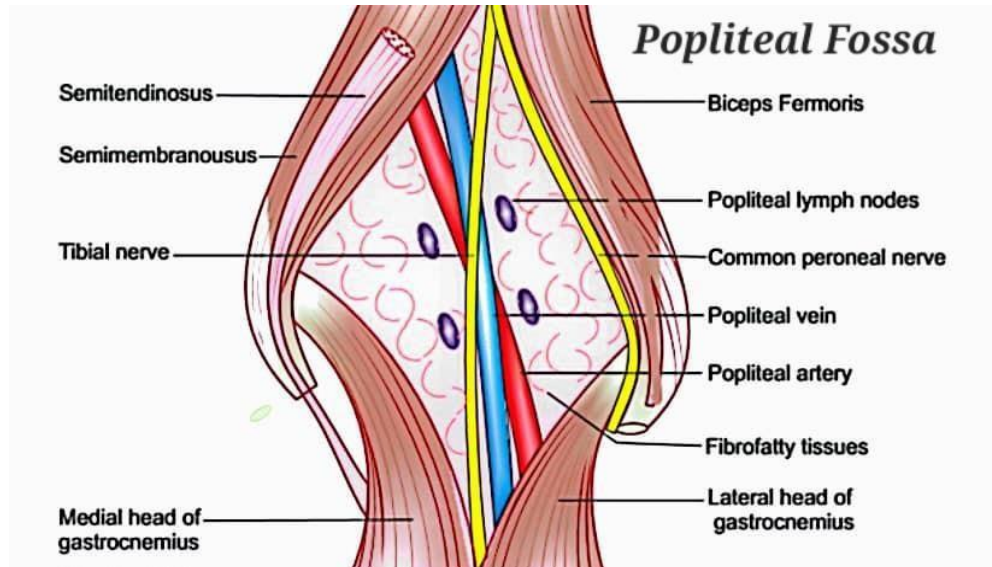
- Saphenous opening (saphenous hiatus, fossa Ovalis) is an oval opening in the upper mid part of Fascia lata of the thigh, lies 3-4-cm below and lateral to pubic tubercle and is about 3cm long.
- Just Inferolateral to the pubic tubercle the fascia extends downwards forming an Arched (Falciform) margin of the lateral boundary of the opening.
- It is covered by a thin perforated Part of the superficial fascia called the fascia cribrosa which is pieced by the great saphenous Opening, the 3 superficial branches of femoral artery and lymphatics.
- The fascia cribrosa/Cribriform fascia must be removed to exposed it.

Structures Passing through Saphenous Opening:

- Great saphenous vein
- Superficial epigastric artery and Superficial external Pudendal artery
- Femoral branch of the Genitofemoral nerve.



LEG	
Anterior Compartment	<ul style="list-style-type: none"> • Muscles: tibialis anterior, extensor hallucis Longus, extensor digitorum longus, and fibularis tertius. • They dorsiflex the foot at the ankle joint, extend the toes, and invert the foot. • All are innervated by the deep fibular/Peroneal nerve, which is a branch of the common fibular nerve. • The compartment most affected in a lower leg compartment syndrome is the anterior compartment and diagnosed by -- Numbness in the web space between the first and the second toes due deep peroneal nerve compression
Lateral Compartment	<ul style="list-style-type: none"> ❖ Fibularis longus and fibularis brevis (also Known as peroneal longus and brevis) ❖ Evert the foot (turn the sole outwards). ❖ innervated by the superficial fibular nerve Which is a branch of the common fibular or common peroneal nerve.
Posterior Compartment	<ul style="list-style-type: none"> ❖ Organized into superficial and deep groups. All are innervated by the tibial nerve. ❖ These muscles mainly plantarflex and invert the foot and flex the toes. ❖ The gastrocnemius muscle is the most superficial largest muscles in the leg. ❖ Gastrocnemius has White Fibers. ❖ <u>Soleus is called 2nd heart / Peripheral Heart.</u> ❖ Superficial Group comprises of Gastrocnemius, Plantaris, and, Soleus ❖ All insert onto the heel (calcaneus) of the foot, and, plantarflex the foot at the Ankle joint. ❖ Deep Group comprises of Popliteus, flexor hallucis Longus, flexor digitorum longus, and tibialis posterior. ❖ The popliteus muscle acts on the knee whereas the other three muscles act mainly on the foot.
POPLITEAL FOSSA	<ul style="list-style-type: none"> ❖ A diamond-shaped space behind the knee joint between muscles in the posterior compartments of the thigh and leg <u>Boundaries:</u> ❖ Upper lateral boundary: Biceps femoris muscle ❖ Upper medial boundary: Semitendinosus and semimembranosus muscles ❖ Two lower boundaries: The head of gastrocnemius muscle ❖ The floor of the fossa is formed by the capsule of the knee joint and adjacent surfaces of the femur and tibia, and by the popliteus muscle. ❖ The roof is formed by deep fascia, which is continuous above with the fascia lata of the Thigh and below with deep fascia of the leg. <u>Contents: From superficial to deep</u> ❖ Tibial nerve ❖ The popliteal vein ❖ The popliteal artery -- <u>deepest structure in the fossa.</u> ❖ Common peroneal nerve is medial to bicep femoris tendon
Trochanteric Anastomosis	<ul style="list-style-type: none"> ❖ Connection b/w Internal iliac and femoral artery, near trochanteric fossa to Supply the head of femur. Formed by: ❖ Superior & inferior gluteal arteries ❖ Medial and lateral circumflex femoral artery (Ascending branches)
Cruciate Anastomosis	<ul style="list-style-type: none"> ❖ Connection between internal iliac and femoral artery at the level of lesser trochanter on the back of femur. Formed by: <ul style="list-style-type: none"> ○ Inferior gluteal artery, ○ Medial and lateral circumflex femoral artery (transverse branch) ○ 1st perforating branch of Profunda femoris artery



Greater sciatic foramina	<ul style="list-style-type: none"> Structures passing through it → Piriformis. Above the Piriformis: Superior gluteal nerve and vessels Superior gluteal nerve exists pelvic cavity via greater sciatic foramina. Below the Piriformis: Sciatic nerve, Inferior gluteal nerve and vessels, Posterior cutaneous nerve of thigh. Pudendal nerve & Pudendal vessels, Nerve to quadratus femoris and obturator internus
Lesser sciatic foramen	<ul style="list-style-type: none"> Formed by sacrotuberous and Sacrospinous ligament. Structures passing through it: <ul style="list-style-type: none"> ➤ Sacrotuberous Ligament ➤ Tendon of obturator internus, ➤ Nerve to obturator internus, Pudendal nerve, Internal Pudendal vessels.

FEMORAL TRIANGLE

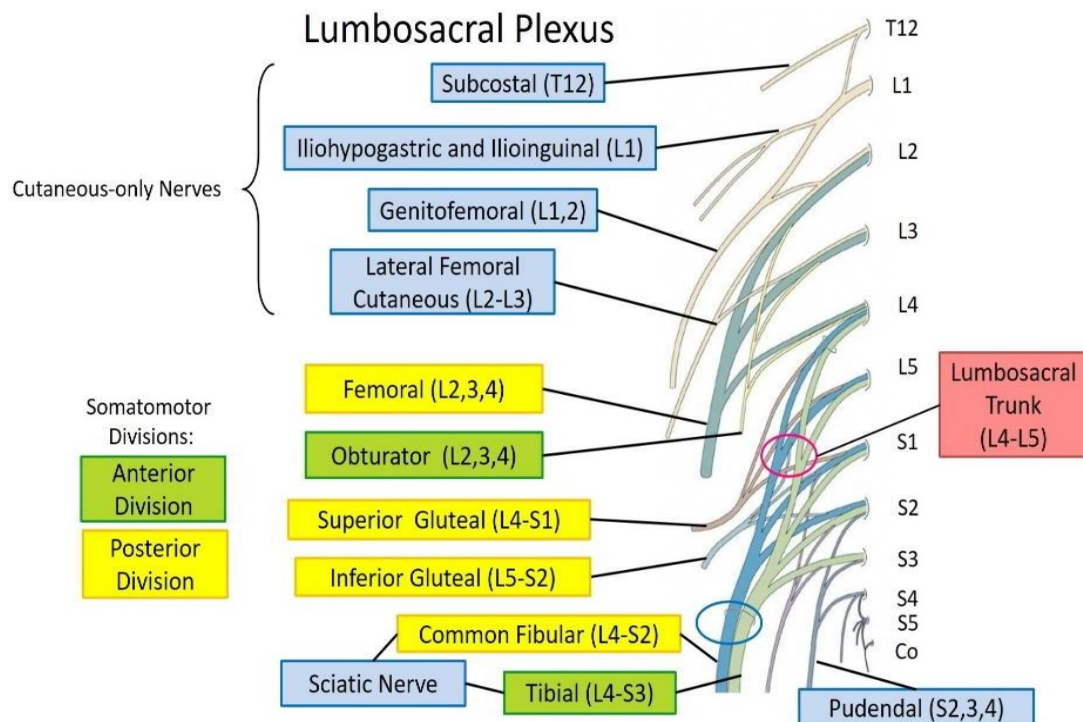
Boundaries	<ul style="list-style-type: none"> Laterally: medial border of Sartorius Medially: medial border of adductor longus Base: inguinal ligament Apex: joining of medial and lateral border
Contents	<ul style="list-style-type: none"> Mnemonics: NAVEL. (NAVEL- from lateral to medial) Femoral Nerve, Femoral Artery, Femoral Vein, Empty space (femoral canal), lymphatics

FEMORAL SHEATH

<ul style="list-style-type: none"> Downward protrusion from abdominal fascia into thigh Anterior wall of sheath: Fascia transversalis Posterior Wall of Sheath: Fascia Iliaca It covers the femoral vessels but not nerve 	Compartments: <ul style="list-style-type: none"> Lateral compartment: Femoral artery Intermediate compartment: Femoral vein Medial compartment: Femoral canal Femoral Ring → Base or upper end of femoral canal is called Femoral ring.
---	---

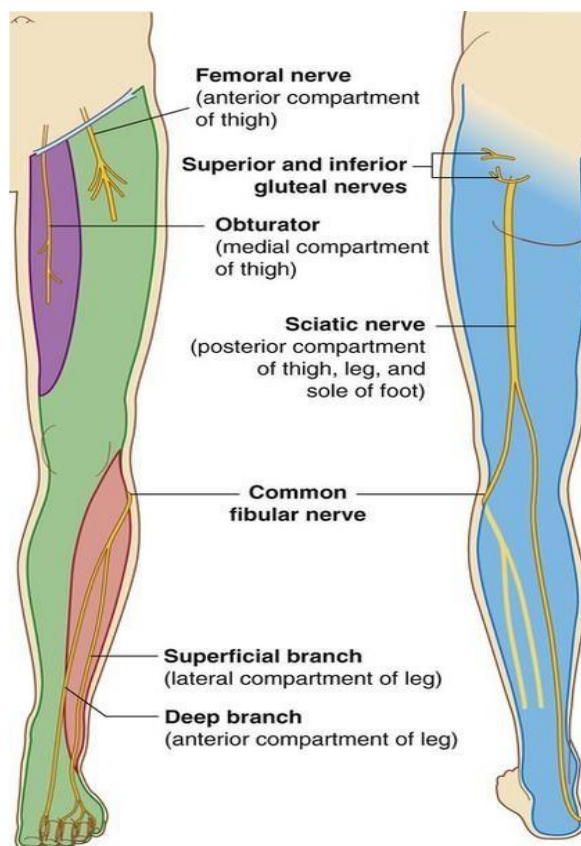
NERVE SUPPLY OF LOWER LIMB	
Lumbar Plexus	<ul style="list-style-type: none"> Formed by Anterior rami of L1- L4, in the substance of psoas muscle in abdomen. Lumbar plexus roots "2 from 1, 2 from 2, 2 from 3": 2 nerves from 1 root <ul style="list-style-type: none"> ilioinguinal (L1) iliohypogastric (L1) 2 nerves from 2 roots: <ul style="list-style-type: none"> Genitofemoral (L1, L2) Lateral Femoral (L2, L3) 2 nerves from 3 roots: <ul style="list-style-type: none"> Obturator (L2, L3, L4) Femoral (L2, L3, L4) Pain referred to inguinal region: ilioinguinal nerve > iliohypogastric involved. Pain referred to Thighs & Testes: Genitofemoral nerve.
Sacral Plexus	<ul style="list-style-type: none"> Lumbosacral plexus → anterior rami of L4- S4: (L4,L5,S1,S2,S3,S4) on Piriformis muscle in pelvis. Divides into Ant & Post Divisions as follows. ✓ Anterior Div → Tibial Nerve, Nerve to Obturator internus, Quadratus femoris, and, inferior gemelli ✓ Posterior div → Common Peroneal, Superior and inf gluteal, femoral nerve, nerve to Piriformis, Perforating Cutaneous nerve. ✓ Mixed → Posterior Cutaneous nerve of thigh (sometimes in Posterior div.)

- Inferior Gluteal nerve** Supplies gluteus Maximus – extensor and anti-gravity muscle.
- Sup glut nerve supplies** Glut Medius + Minimus – abductors + medial rotators



Femoral Nerve L2, L3, L4	<ul style="list-style-type: none"> ❖ Posterior division of primary ventral rami of L2, L3, L4. Branches include: ❖ Anterior cutaneous branches ---supply skin on the front of the Thigh and knee ❖ motor nerves, which supply the quadriceps femoris muscles (rectus femoris, Vastus lateralis, vastusintermedius, vastus medialis muscles) and the Sartorius. ❖ The saphenous nerve (Long cutaneous terminal branch) supplies skin as far Distally as the medial side of knee leg and foot <p><u>Clinical Anatomy:</u></p> <ul style="list-style-type: none"> ❖ Trauma to femoral triangle/ pelvic fracture leads to injury of femoral nerve resulting in Weak flexion of thigh, extension of leg is lost, sensory loss on anterior Thigh and medial leg. Loss of knee jerk + anaesthesia on anterior thigh 		
Obturator Nerve L2, L3, L4	<ul style="list-style-type: none"> ❖ branch of Lumbar plexus, from anterior div of primary ventral rami of L2, L3, L4. ❖ It passes within the psoas muscle, emerges from the Medial surface of the psoas, passes posteriorly to the common iliac artery and medially to the Internal artery at the pelvic inlet, and then courses along the lateral pelvic wall. It leaves the pelvic Cavity by traveling through the obturator canal ❖ Supplies medial/adductor compartment of thigh. ❖ Injury may occur in: Anterior dislocation of hip joint, mostly 2cm below and lateral to pubic tubercle, Radical retropubic prostatectomy ❖ Injury results in: Adduction of thigh is lost + Sensory loss on medial thigh 		
SCIATIC NERVE L4 – S3	<ul style="list-style-type: none"> • The largest + thickest nerve of the body + key nerve of lumbosacral plexus. • Forms on the anterior surface of the piriformis muscle and leaves the pelvic cavity through the Greater sciatic foramen inferior to piriformis • In the thigh, it divides into its two major branches: <ol style="list-style-type: none"> 1. Common fibular/Common Peroneal nerve: Formed by Posterior division of L4-S2 2. Tibial nerve: Formed by Anterior division of L4-S3 		
Common Peroneal Nerve L4 – S2	<ul style="list-style-type: none"> • Common Peroneal /Common Fibular Nerve, L4-S2 • Smaller Terminal branch of sciatic nerve that is Easily palpable medial to bicep femoris tendon and supplies all muscles of anterior and lateral leg compartments • Supplies short head of bicep muscle in posterior compartment of thigh , Extensor digitorum brevis in the foot (also contributes to the supply of the first dorsal Interosseous muscle) • Skin on the anterolateral surface of the leg and dorsal surface of the foot • PED = Peroneal causes → Eversion and Dorsiflexion • Divides into superficial and deep peroneal nerve • Blow to lateral aspects of leg/ Fracture of neck of fibula results in injury to CPN & Anterior tibial artery. • If want to get the marrow biopsy we need to enter from medial side than on lateralside in Order to save common peroneal from injury. <p><u>Common peroneal nerve injury causes:</u></p> <ul style="list-style-type: none"> • Foot drop and inversion (eversion of foot is lost) • Dorsiflexion of foot and Extension of toes is lost • Sensory loss on anterolateral leg and dorsum of foot • Common peroneal nerve and anterior tibial artery are involved in anterior Compartment Syndrome . • Clinically Patient presents with planter flexed (Foot drop) & inverted foot and can't stand on heels "foot slap" <table border="1" data-bbox="454 1803 1428 2031"> <tr> <td data-bbox="454 1803 702 2031"> Superficial peroneal Nerve </td><td data-bbox="702 1803 1428 2031"> <ul style="list-style-type: none"> • Terminal branch of CPN, Supply the lateral compartment, muscle, and, skin over the dorsum of foot between 1st and 2nd digits. • If dorsum of foot is not supplied by sciatic nerve, then it will be supplied by saphenous Nerve, a terminal branch of femoral nerve. • Injury causes Inversion of foot (Loss of eversion) </td></tr> </table>	Superficial peroneal Nerve	<ul style="list-style-type: none"> • Terminal branch of CPN, Supply the lateral compartment, muscle, and, skin over the dorsum of foot between 1st and 2nd digits. • If dorsum of foot is not supplied by sciatic nerve, then it will be supplied by saphenous Nerve, a terminal branch of femoral nerve. • Injury causes Inversion of foot (Loss of eversion)
Superficial peroneal Nerve	<ul style="list-style-type: none"> • Terminal branch of CPN, Supply the lateral compartment, muscle, and, skin over the dorsum of foot between 1st and 2nd digits. • If dorsum of foot is not supplied by sciatic nerve, then it will be supplied by saphenous Nerve, a terminal branch of femoral nerve. • Injury causes Inversion of foot (Loss of eversion) 		

	Deep peroneal nerve	<ul style="list-style-type: none">Supply anterior compartment of leg and enters dorsum of foot by passing deep to extensor retinaculum on the lateral Side of the dorsalis Pedis artery.Injury to deep peroneal Nerve cause Foot drop					
Tibial Nerve L4 – S3	<ul style="list-style-type: none">large terminal branch of sciatic that arises in lower third of thigh and enters posterior Compartment of thigh.Supplies All muscles in the posterior/ hamstring compartment of the thigh and post compartment of Leg also.(Hamstring part of the adductor magnus) except for the short head of the biceps which is supplied by common peroneal nerve)All muscles in the sole of the foot are supplied by TN.Sensory (cutaneous) function: Skin on posterolateral and medial surfaces of foot and sole of foot (plantar aspect of foot)Function: TIP---Tibial nerve causes Inversion and Plantar flexionCommonly injured in knee trauma and lesion causes Dorsiflexion and eversion of foot at Subtalar and trans tarsal Joints with loss of inversion.Branches are as follows: <table><tr><td>Medial plantar nerve</td><td><ul style="list-style-type: none">Arise beneath flexor retinaculum and like median nerve it supplies LOAF muscle – Lumbricals, Opponens, abductors, and flexors of toes.Supplies medial 3 and half toes</td></tr><tr><td>Lateral plantar nerve</td><td><ul style="list-style-type: none">Ulnar nerve like distribution , arise beneath flexor retinaculum to Supply all interosseous and lumbrical muscles except first lumbrical</td></tr></table>			Medial plantar nerve	<ul style="list-style-type: none">Arise beneath flexor retinaculum and like median nerve it supplies LOAF muscle – Lumbricals, Opponens, abductors, and flexors of toes.Supplies medial 3 and half toes	Lateral plantar nerve	<ul style="list-style-type: none">Ulnar nerve like distribution , arise beneath flexor retinaculum to Supply all interosseous and lumbrical muscles except first lumbrical
Medial plantar nerve	<ul style="list-style-type: none">Arise beneath flexor retinaculum and like median nerve it supplies LOAF muscle – Lumbricals, Opponens, abductors, and flexors of toes.Supplies medial 3 and half toes						
Lateral plantar nerve	<ul style="list-style-type: none">Ulnar nerve like distribution , arise beneath flexor retinaculum to Supply all interosseous and lumbrical muscles except first lumbrical						



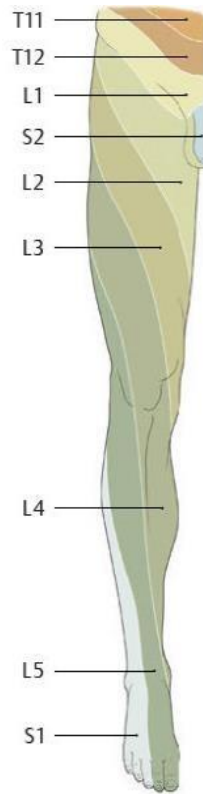
BLOOD SUPPLY & VENOUS DRAINAGE OF LOWER LIMB

Artery	Course & Features	Branches
Femoral Artery	<ul style="list-style-type: none"> Continuation of External iliac artery. Major artery supplying lower Limb. Enters thigh behind the inguinal ligament Palpated at MID-INGUINAL point. Aneurysm presents as a Pulsatile mass below inguinal Ligament. 	<ul style="list-style-type: none"> Superficial circumflex iliac artery Superficial epigastric artery Superficial external pudendal artery Deep external pudendal artery Profunda femoris artery : largest branch, it gives: Medial, and Lateral Circumflex arteries, 3 branches of Perforating arteries and ends as 4th perforating artery.
Popliteal Artery	<ul style="list-style-type: none"> Popliteal Artery is the continuation of Femoral artery and enters Popliteal fossa through an opening in Adductor magnus. Most deeply and anteriorly placed in popliteal Fossa Supracondylar fracture of femur can harm it Pain after walking 100 yards indicates Popliteal artery disease. 	<p>At lower end of Popliteus, it divides into: Anterior tibial artery and posterior tibial artery.</p> <p>Anterior Tibial artery:</p> <ul style="list-style-type: none"> One of the terminal branches of popliteal artery, begins at level of lower border of the popliteus muscle and lies superficial in front of lower end of tibia, passes behind the superior extensor retinaculum, it has the tendon of the extensor Hallucis longus on medial side and the tendon of extensor digitorum longus on lateral side. It is here that its pulsation can easily be felt. Commonly injured in neck of fibular fracture In front of ankle, this artery becomes dorsalis pedis artery. <p>Posterior tibial artery:</p> <ul style="list-style-type: none"> One of the smaller terminal branches of popliteal artery that Begins at the level of lower border of the popliteus. The pulse of artery is palpable Midway between the medial malleolus and the heel as it is covered here only by a thin layer of retinaculum, by superficial Connective tissue, and by skin. The artery passes behind the medial malleolus deep to the flexor retinaculum and terminate by Dividing into Medial plantar arteries and Lateral plantar arteries
Dorsalis Pedis artery	<ul style="list-style-type: none"> Terminal branch of anterior tibial artery that passes through 1st and 2nd metatarsal space and Absent in some children If absent , alternate is perforating branches of peroneal artery or accessory peroneal artery. Maximum pulse pressure and maximum amplitude at Dorsalis Pedis artery The pulse of the dorsalis pedis artery on the dorsal surface of the foot can be felt by gently palpating the vessel against the underlying tarsal bones between the tendons of extensor hallucis longus and the tendon of extensor digitorum longus to the 2nd toe 	
Medial Plantar	<ul style="list-style-type: none"> Smaller Terminal Branch of Medial of The Posterior Tibial Artery Supplies The Medial Side of The Big Toe 	
Lateral Plantar	<ul style="list-style-type: none"> larger of the terminal branch of the posterior tibial artery At the fifth metatarsal bone, the artery curve medially and form the plantar Arch. At the first intermetatarsal space joint the dorsalis pedis artery 	

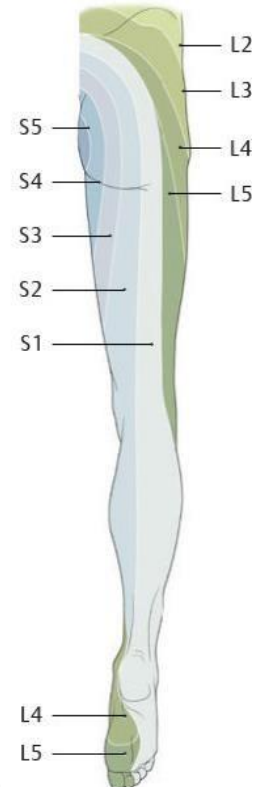
Vein	Tributaries	Clinical Anatomy
<p>Greater Saphenous Vein</p> <ul style="list-style-type: none"> longest vein in the body, has 20 valves, it is located 2.5cm anterior to medial malleolus. It Ascends with saphenous nerve in the superficial fascia over the medial side of the leg. Pass behind the knee and then on medial side of the thigh Enter the saphenous opening. Ends by Joining the femoral vein about 4 cm below and lateral to pubic tubercle. Perforator connects the superficial veins with deep veins, which are not present at below inguinal ligament 	<ol style="list-style-type: none"> Medial marginal vein of big toe Anterior vein of leg superficial Dorsal vein of penis deep dorsal vein of penis drains into prostatic venous Plexus also known as Santorini's plexus. Drains the medial side of the dorsolateral arch of the foot. Superficial epigastric vein Superficial circumflex iliac vein The external pudendal veins (deep Pudendal & superficial pudendal) are veins of the pelvis, which drain into the great saphenous vein. Deep external pudendal vein (last tributary) empties the blood from the anterior part of the perineum. <p>Does Not receive vein from deep vein of calf.</p>	<ul style="list-style-type: none"> Located in front of medial malleolus. Can be used for emergency blood Transfusion and this is also the site for saphenous nerve in front of the vein. So, during the cut-down process, the saphenous nerve ought to be recognized to avert injury. vein graft: In coronary bypass surgery to ease the ischemia of the heart, a Section of great saphenous vein is removed and utilized for aortocoronary grafting. There are about 5-perforator vein along the great saphenous vein 1. mid thigh, 2 below knee, 3, 5 near the lower leg and ankle. Great saphenous vein itself drain into femoral vein
<p>Small Saphenous Vein</p> <ul style="list-style-type: none"> Arise from lateral part of the dorsolateral arch It ascends behind the lateral malleolus in company with sural nerve 	<ul style="list-style-type: none"> It runs in the middle of the back of leg. The vein pierces the deep fascia and passes between the head of gastrocnemius muscle in the lower Part of the popliteal fossa. it ends in popliteal vein 	<ul style="list-style-type: none"> Posteromedial femoral vein is some time called accessory saphenous vein. Relation with Sural nerve is important.

LYMPHATIC DRAINAGE

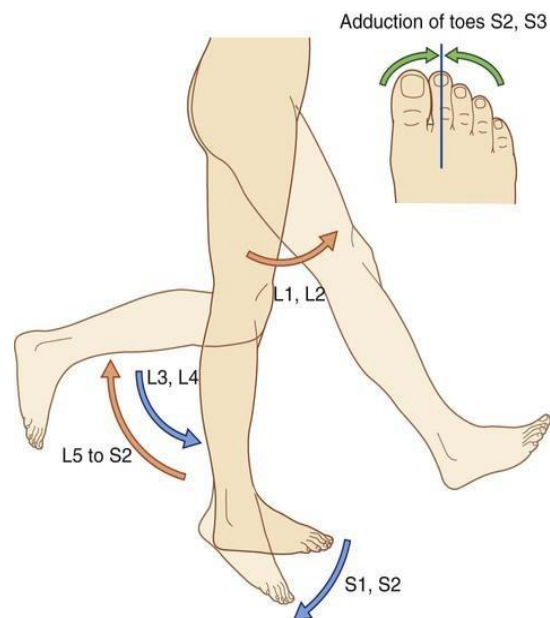
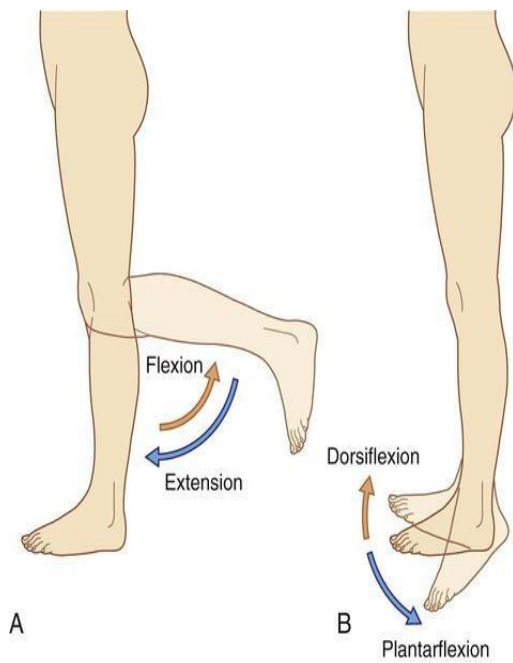
Deep inguinal L.Ns	They Drain glans of penis and corpora + Clitoris	
Superficial inguinal L.Ns	Pass through saphenous opening and drain into deep inguinal lymph node and finally to External iliac nodes. It has Vertical & Horizontal groups.	
	Vertical group	Receives lymph from vessels of lower limb
	Horizontal group	<p>It has Lateral & Medial groups.</p> <ul style="list-style-type: none">○ Lateral group Receives lymph from the back below the iliac crests.○ Medial group Drains from<ul style="list-style-type: none">➤ anterior abdominal wall at the level of umbilicus➤ perineum➤ area below hymen,➤ Lower half of anal canal below pectinate line.➤ Uterus (Partially to superficial inguinal node)➤ Scrotum
Popliteal nodes	<p>They receive lymph from superficial Vessels, which accompany the small saphenous vein, and from deep areas of the leg and Lateral Foot.</p> <p>They ultimately drain into the deep and superficial inguinal nodes</p>	



A Anterior view.



B Posterior view.



Dermatomes and Myotomes of Lower Limb			
T12	Lower abdomen, upper buttock	L2 – L3 (Lift my knee)	Hip flexion (L2)
L1	Suprapubic + inguinal region Penis, anteroscrotum (labia) Upper buttock L1 → inguinal ligament (BCQ)	L3 – L4 (kick the door) Knee jerk/patellar tendon reflex L3 – hip extension + knee flexion	Knee extension Knee jerk: L3 > L4 (BCQ)
L2	Anterior thigh, upper buttock	L4 – L5 (Foot points to the sky)	Dorsiflexion
L3	Anterior and medial thigh + knee	L4 – L5 (I extend my thigh)	Hip extension
L4	Medial leg, medial ankle, and side of foot L4 → Medial malleolus (BCQ) Skin around knee + knee cap → L3	L5 – S1 (I kick my bum)	Knee flexion
L5	Lateral leg, dorsum of foot, medial sole Big Toe → L5 (BCQ)	S1 – S2 (stand on my shoes)	Plantar flexion (S1*)
S1	Lateral ankle, lateral side of dorsum and sole Lateral foot and small toe dermatome → S1	L2-L3-L4 (modesty closes the door)	Hip adduction
S2	Posterior leg, posterior thigh, buttock, penis	L5-S1-S2 (The opposite is true)	Hip abduction
S3	Sitting area of buttock, Posterior scrotum (labia)	L4 - the medial side lifts off the floor	Foot inversion
S4	Peri anal region and perineum /genitals	L5/S1 – lateral side points upto sun	Foot eversion
S5	S5 & Coccyx: Behind anus and over coccyx	S1/S2	Ankle jerk (S1)

- **Stand on S1, Squat on S2 ; Sit on S3**
- L2 – hip flexion
- L3 – hip flexion, knee extension
- **L4 – knee extension, ankle dorsiflexion, foot inversion**
- L5 – hip extension, knee flexion, ankle dorsiflexion, foot inversion & eversion
- S1 – hip extension, knee flexion, **ankle Plantarflexion**, foot eversion
- S1/S2 – ankle Plantarflexion

Cremasteric reflex (L1, L2)

- Superficial reflex, Polysynaptic.
- Afferents: Genitofemoral (femoral branch) & Ilioinguinal nerve
- Efferents: Genitofemoral nerve (genital branch)
- Overall imp: **Genitofemoral Nerve**

In Newborn

- Upper limb well developed and Lower limb less developed
- C shaped vertebral column
- Inner ear is of same size as that of adult
- Thorax of newborn is circular, and adult is oval shaped.
- Blood Vol is 80-85 ml/kg.

PAST PAPERS BCQs

1. Commonest fracture in the lower limb is fracture of neck of femur
2. Most dislocated bone in the lower limb is Patella
3. Most common neuropathy in the lower limb is compression of common peroneal nerve against neck of fibula
4. Longest muscle in the body is Sartorius. Thickest nerve in the body is Sciatic nerve
5. Largest bone of the body is Femur. Largest & most complicated joint in the body is knee joint
6. Largest sesamoid bone in body is Patella
7. Strongest ligament in the body is iliofemoral ligament
8. Strongest tendon in the body is Tendo calcaneus
9. Largest synovial cavity in the body is synovial cavity of the knee joint
10. Most commonly nerve used in the body for grafting is Sural nerve
11. Most used vein in body for grafting is Great saphenous vein
12. Most used muscle in the body for grafting is Plantaris & Palmaris longus
13. Locking muscle for knee is Quadriceps Femoris. Unlocking muscle for knee is Popliteus
14. Tears of anterior cruciate ligament are more common than posterior
15. Tears of medial collateral ligament are more common than lateral
16. Acute sprains of lateral ankle are more common than medial Ankle
17. Saphenous nerve accompanies Great saphenous vein. Sural nerve accompanies small saphenous vein.
18. Deep peroneal nerve accompanies anterior tibial artery
19. Most common hip dislocation :Posterior
20. Most common ligament tear of knee : MCL
21. Medial longitudinal arch of foot : Talus. Transverse arch of foot : Cuneiform bones
22. Most common fractured bone in lower limb : Tibia
23. Hip dislocated : leg internally rotated and adducted
24. Fracture of neck of femur → leg externally rotated, Abducted, and shortened.
25. Abduction of hip joint limited by : Pubofemoral ligament
26. Extension of hip joint limited by : iliofemoral ligament
27. Flexion of hip joint with knee extended is limited by hamstring muscles
28. Flexion of hip joint with knee flexed is limited by anterior abdominal wall
29. Football player tackled from lateral side on the knee structures injured : Unhappy triad
30. 1.Medialmeniscus , 2.Tibial collateral ligament , ACL are injured
31. Cuneiform forms : transverse arch of foot
32. Talus has no muscular attachment. Nerve affected in tarsal tunnel syndrome : tibial
33. ACL Prevents Anterior dislocation of Tibia on femur
34. ACL prevents : Posterior dislocation of femur on tibia
35. Most common type of injury →Inversion-Lateral ligament damage
36. Most common subtype of lateral Ligament →Anterior talofibular ligament
37. Forced eversion of the foot avulses the medial malleolus or ruptures the deltoid ligament
38. Whereas forced inversion avulses the lateral malleolus or tears the lateral collateral(anterior, posterior talofibular and calcaneo fibular) ligament.
39. Ankle sprain (inversion injury) results from rupture of Calcaneofibular and talofibular ligament and a fracture of the lateral malleolus caused by forced inversion of the foot.
40. The most common ankle sprain consists of an inversion injury of the foot with some degree of plantarflexion.
41. Stability of ankle joint doesn't depend on : Calcaneonavicular(spring ligament)
42. The Commonest Neuropathy related to Childbirth : Meralgia paresthetica.
43. (it is the Neuropathy of the Lateral Femoral Cutaneous Nerve).
44. Flex thigh flex knee : Sartorius muscle
45. Sole of foot sensory supply : Tibial nerve. Dorsum of foot sensory supply – superficial peroneal nerve.
46. Space between 1 st and 2 nd toe of lower limb sensory supply deep peroneal nerve.
47. Pain felt between great toe and 2 nd toe is due to involvement of which nerve root : L5
48. Ant tibial Nerve damaged Muscle spared → Short head of Bicep femoris.

THORAX

- The shape of thorax varies with age. In newborn infant, the thorax is round when view from Above, but with increasing age, it become more oval and appears flatter anteriorly & posteriorly.
- Spine of newborn is C-shaped.
- Thorax contains imp Vital Organs i.e., Heart , Lungs, Vasculature, and ducts (Aorta, IVC, Thoracic duct).

CHEST WALL	
Thoracic Wall layers	<ol style="list-style-type: none"> 1. Skin 2. Superficial Fascia 3. External Intercostal Muscle 4. Internal Intercostal Muscle 5. Innermost Intercostal Muscle 6. Endothoracic Fascia (thin layer of loose connective tissue separating parietal pleura from chest wall) 7. Parietal Pleura 8. Visceral Pleura 9. Lungs
Ribs and Sternum	<ul style="list-style-type: none"> • The first rib articulates with sternum near the Sternoclavicular Joint. • The Angle of the rib is the most common site of rib fracture. • Sternum is the most common site for marrow biopsy in adults, but preferred site is Ventral iliac crest. The body, also called the blade or Gladiolus, is right in the middle of the sternum. The Sternum body ossify at age of 25. • Sternum starts Hematopoiesis after 21 years of age. • Sternal Angle • Also known as the angle of Louis or manubriosternal junction is the synarthrotic joint formed by the articulation of the manubrium and the body of the sternum • Union of manubrium and body at 2nd rib • The sternal angle can be palpated at the T4 vertebral level. • Ribs & costal cartilages are calculated from this angle. • Structure at the level of the angle of Louis: • 2nd costal cartilage • Ascending Aorta ends, arch of the aorta begins and ends, Descending aorta begins, • tracheal bifurcation , Pulmonary trunk bifurcation • Boundary b/w superior and inferior mediastinum • Azygous vein ends into SVC, Recurrent laryngeal nerve Loops around arch of aorta. • RIBS (12 pairs) • True ribs: The upper seven are attached anteriorly to the sternum by their costal cartilage. • False ribs: The 8th, 9th and 10th pairs of rib attached to each other and to the 7th ribs by means of Their costal cartilage and small synovial joint. • Floating ribs: The 11th and 12th pairs have no anterior attachment
Cervical Rib	<ul style="list-style-type: none"> • Arises from the anterior tubercle of the transverse process of the C7. May be connected to the first rib by a fibrous band, or may articulate with the first rib, which causes pressure on the lower trunk of brachial plexus Especially T1 and the subclavian artery. • Symptoms include Paraesthesia/Numbness and tingling sensations at Ulnar/Medial border of Hand. • Key to Remember - cervical rib Arises from C7 & Compresses T1.
Suprapleural membrane	<ul style="list-style-type: none"> • Also called Sibson's Fascia (The thickening of Endothoracic fascia) • It attaches to the internal border of first rib and transverse processes of C7. • Protects apex of lung, and, also prevents the Apex to Pop out during inspiration.
Innervation of chest wall	<ul style="list-style-type: none"> • Above the level of the sternal angle : Supraclavicular nerve (C3-C4) • Below the level of sternal angle: The anterior and lateral cutaneous branch of the Intercostal nerve • Posteriorly : The posterior rami of the spinal nerves

PLEURA

- Normal lung pleura is composed of fibrous connective tissue lined by mesothelium.
- 1. **Parietal pleura:** it is sensitive to Pain, Pressure, temperature, touch and supplied as follows:
 - a. Costal pleura is supplied by Intercostal nerve only.
 - b. Mediastinal pleura by : Phrenic nerve only (Only mediastinal Pleura is totally dependent on Phrenic nerve)
 - c. Diaphragmatic pleura : Supplied over the dome by phrenic nerve and around the Periphery by the lower six intercostal nerve.
- 2. **Visceral pleura:** Covering the lung and is sensitive to stretch only, it receives an autonomic nerve Supply from the pulmonary plexus .
- **Negative Intrapleural pressure is due to lymphatic drainage of pleura.**

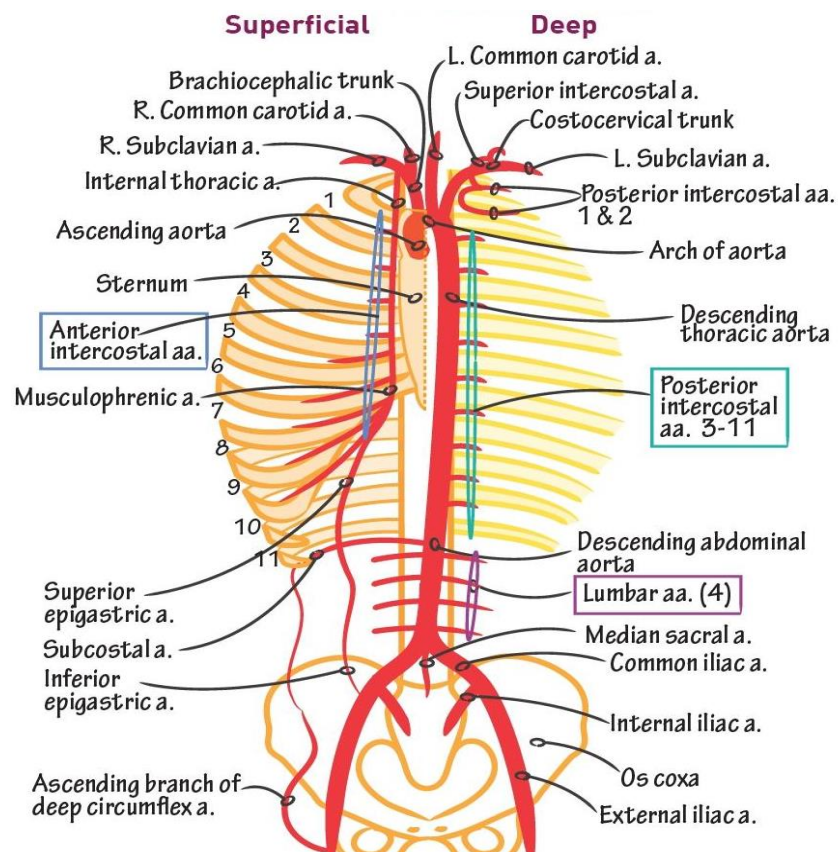
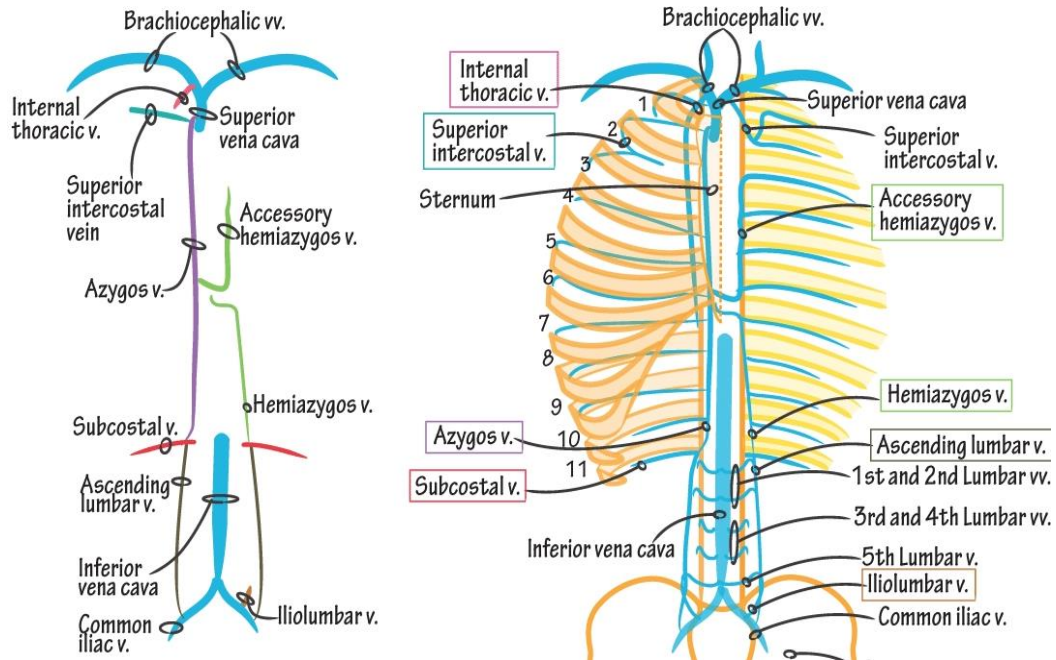
INTERCOSTAL SPACES

Blood Supply	<p>Each Intercostal Space Contains a Large Single Posterior Intercostal Artery and Two Small Anterior Intercostal Arteries.</p> <p><u>Anterior Intercostal Arteries</u></p> <ul style="list-style-type: none"> ❖ 1 – 6th spaces arise from → Internal Thoracic Artery, which Arises from the First Part of The Subclavian Artery. ❖ The Lower Spaces 7th – 9th arise from Musculophrenic Artery, (One of the Terminal Branches of The Internal Thoracic Artery) ❖ 10th and 11th space : No anterior intercostal artery supply. <p><u>Posterior Intercostal Arteries:</u> (Superior intercostal artery + descending thoracic aorta)</p> <ul style="list-style-type: none"> ❖ 1st and 2nd arise from Superior Intercostal Artery (Branch of The Costocervical Trunk of The Subclavian Artery) ❖ Lower Nine Spaces (4 – 11th) arise from the Descending Thoracic Aorta <p><u>Bronchial Artery</u></p> <ul style="list-style-type: none"> ✓ Bronchial artery arises at The Level of T5-T6 ✓ Bronchial Artery is One on The Right Side and are two on the Left Side ✓ Left Bronchial Arteries (Superior and Inferior) Usually Arise from Thoracic Aorta. ✓ Single Right Bronchial Artery Arises from Third Right Posterior intercostal artery.
Intercostal veins	<ul style="list-style-type: none"> ❖ Thoracic wall → Total 11 Intercostal veins ❖ Veins of all Anterior intercostal spaces → arise from Internal thoracic vein ❖ Posterior intercostal spaces : 1st space – Brachiocephalic vein ❖ 2nd – 4th posterior intercostal veins : from Superior intercostal vein ❖ 4th – 11th posterior intercostal veins : from
Brachiocephalic Vein	<ul style="list-style-type: none"> • Brachiocephalic Vein Is Formed by The Union of The Internal Jugular Vein and Subclavian Vein Behind the Sternoclavicular Joints (Behind the Medial/Sternal End of The Clavicle) • SVC Is Formed by The Union of The Right and Left Brachiocephalic Veins • Right Brachiocephalic Vein : Shorter, 1 Inch Long , Phrenic Nerve on Its Right Side While Innominate Artery on Left. • In Obstruction of The Upper Inferior Vena Cava, The Azygous and Hemiazygos Veins and Vertebral Plexus Are the Channels Collateral Maintaining Venous Circulation • Left Brachiocephalic Vein: Longer, 2.5 Inch , Oblique Course • Anterior: Manubrium, posteriorly: Branch of The Aortic Arch, Trachea and Left Vagus Nerve, Aortic Arch Inferiorly • Lt Brachiocephalic Vein Receives → Inferior Thyroid Vein, Inferior Thymic Vein, Thoracic Duct, Superior Intercostal Vein
Azygos vein	<ul style="list-style-type: none"> • An Unpaired Vein Formed by The Union of Right Ascending Lumbar Vein and The Right Costal Vein • Empties Into the Posterior Surface of SVC Inside the Pericardium

	<ul style="list-style-type: none"> ✚ If IVC Is Blocked Just Above the Emergence of Azygos Vein : Blood Will Be Diverted into Azygous Vein ✚ IVC Is Blocked Up to Extent of Azygos Vein : Blood Will Divert into Right Ascending Lumbar Vein & Rt Subcostal. ✚ Obstruction Of IVC Before Azygous Vein Emergence : Blood Will Be Diverted to Azygous Vein, Right Ascending Lumbar and Right Subcostal Vein. <p><u>Tributaries</u></p> <ul style="list-style-type: none"> • 8 Lower Intercostal Vein, Right Superior Intercostal Vein • Superior And Inferior Hemiazygos Vein , Mediastinal Veins • All Posterior Intercostal Vein Except 1st Vein
Hemiazygos vein	<ul style="list-style-type: none"> • Inferior HV Formed by The Union of Left Ascending Lumbar Vein and The Left Subcostal Vein • Turn To the Right and Join the Azygos Vein in Front of T9 • Superior HV Formed by The Union of the 4th – 8th Intercostal Vein • It Joins the Azygos Vein at T 7.
Neurovascular bundle	<p>The inferior border of the superior rib forms the “Coastal groove” which has Neurovascular bundle. The intercostal drainage tube should be inserted along the superior Surface of the inferior rib (lower border of intercostal space). Must enter the chest Over the rib, not under it.</p> <ul style="list-style-type: none"> • From superior/above to inferior/downward : VAN Intercostal Vein, intercostal Artery, and Intercostal Nerve • Intercostal nerve is at higher risk of injury. • Neurovascular bundle is Located between internal and innermost layer.
For Pleural Tap & Intercostal nerve block	<p>insert needle into the Upper border of the lower rib and the lower part of intercostal space for pleural tap.</p> <p>For intercostal nerve block → Insert the needle onto lower border of rib & upper part of intercostal space.</p> <p>So, the pleural tap and nerve block are opposite to each other.</p>
Muscles	<p>Intercostal muscles form the wall proper of the thorax.</p>
Intercostal nerves	<ul style="list-style-type: none"> • The intercostal nerves are part of the somatic nervous system and arise from the anterior Rami of the thoracic spinal nerves from T1 to T11. • Each pursues an independent course without plexus formation. • The first two nerves supply fibres to the upper limb in addition to their thoracic branches. • The next four are limited in their distribution to the walls of the thorax; the lower five supply the walls of the thorax and abdomen. • The 7th intercostal nerve terminates at the xiphoid process, at the lower sternum. • The 10th intercostal nerve terminates at the umbilicus (T10) • The twelfth (subcostal) thoracic is distributed to the abdominal wall and groin. • The lateral cutaneous branch of the second intercostal nerve does not divide, like the others, into an anterior and a posterior branch. it is named the Intercostobrachial nerve.
Intercostobrachial nerve (T2 – cutaneous branch)	<ul style="list-style-type: none"> • A lateral cutaneous branch of the second intercostal Nerve that supplies sensation to the skin of the axilla. • it leaves the second intercostal space at the midaxillary line and subsequently pierces the Serratus anterior muscle to enter the Subcutaneous tissues of the axilla. • It traverses the axillary lymph nodes and is often divided during axillary surgery. • Pain of MI is carried to Left Arm by Intercostobrachial nerve, supplying that area.

Structure Damaged in Penetrating Injury to the Chest

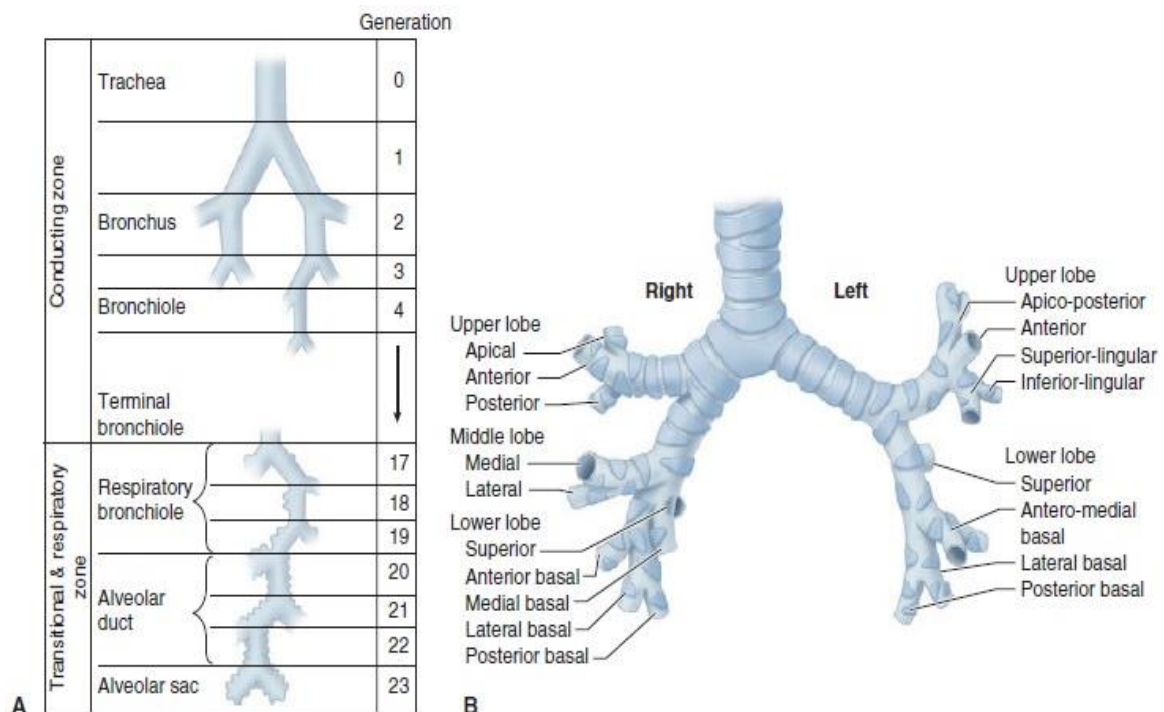
- Injury at 4th intercostal space to the left of sternum damages = intercostal membrane (inner)
- Injury or stab wound at 5th intercostal space to the left of sternum damages = Intercostal muscle
- Stab wound left chest 5cm, 4 inches deep just lateral to sternum will involve/damage = Pericardium
- Injury at 6th intercostal space damages = IVC
- Injury at 6th costal cartilage right of sternum / xiphisternum damages = Right Atrium
- A stab wound in chest starts at and including external intercostal muscle and (parietal pleura and pleural cavity as 2 layers). It will pierce how many layers = 8



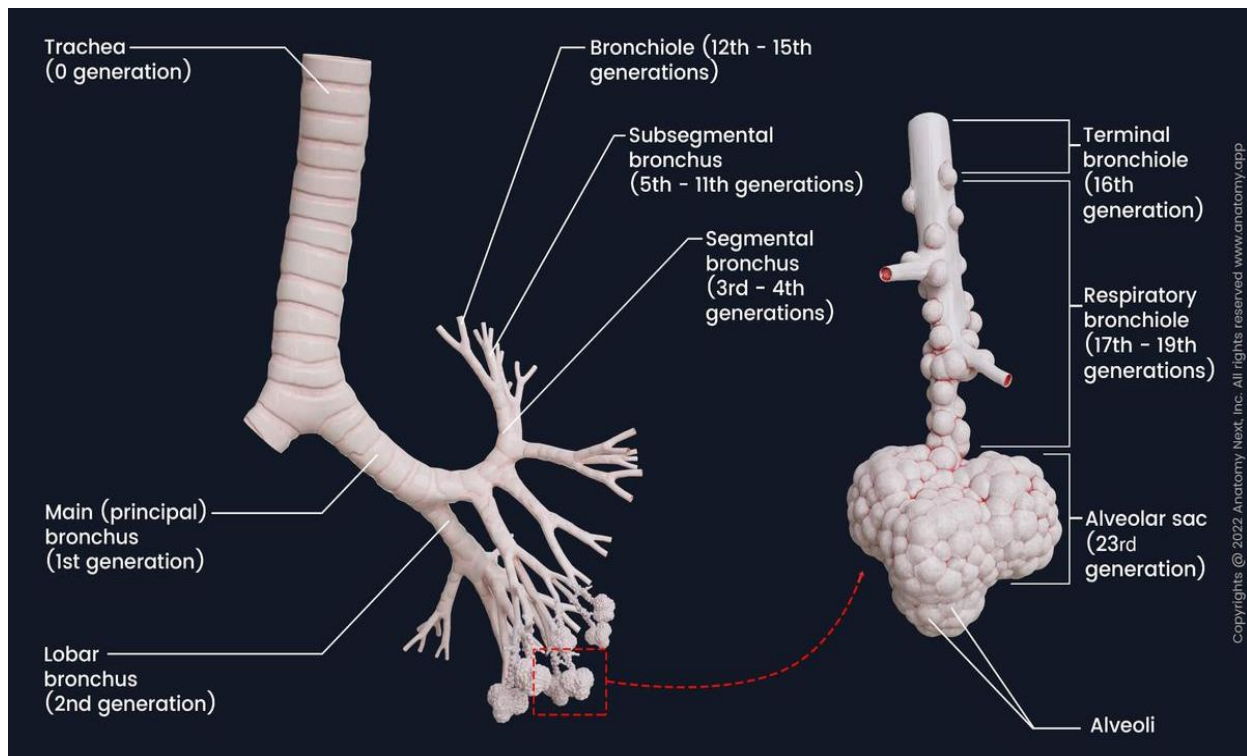
TRACHEA & LUNGS	
Trachea	<ul style="list-style-type: none"> ❖ Epithelium: Pseudostratified columnar ciliated epithelium with goblet cell ❖ Trachea is the continuation of the larynx ,begins at the lower border of the cricoid at C6 and bifurcates at T4/T5 or upper Border of L5 ❖ Size of the trachea in neonate is 4 cm and in adult 10 cm. Laryngotracheal bud appears during 4th week ❖ 16-20 incomplete rings of C-shaped hyaline cartilage, arranged on anterior aspect of the trachea. ❖ The gap between Posterior end is filled with Trachealis muscle, contraction of Trachealis decreases trachea diameter. ❖ Carina is a keel-like ridge in the lumen in the bifurcation of the trachea or Anterior-posterior Cartilage at the bifurcation of trachea .The mucosa of trachea over the carina is most sensitive. The cough reflex is generally Started here, which helps to clear sputum. Tracheostomy is not beneficial if the lesion is at carina.
Relations of Trachea	<ul style="list-style-type: none"> ❖ Anterior: Arch of aorta , Brachiocephalic trunk , left common carotid artery ,Left brachiocephalic vein and Deep cardiac plexus ❖ Posterior: Esophagus, left recurrent laryngeal nerve (ascends between trachea and esophagus) ❖ To the right: lateral to the trachea : Right vagus nerve (close contact) , Azygos vein ❖ To the left: lateral to the trachea →Left vagus nerve (close contact) , Arch of aorta , left common carotid artery , left subclavian vein , Left phrenic nerve. <p>Imp Concept :</p> <ul style="list-style-type: none"> ❖ Vagus Nerve is in direct contact with trachea ❖ Recurrent laryngeal nerve lies immediately lateral to trachea
Blood Supply	<ul style="list-style-type: none"> • Upper 2/3rd trachea: inferior thyroid artery • Lower 1/3rd : branch of the bronchial artery • Venous drainage: inferior thyroid plexus
Nerve supply	<ul style="list-style-type: none"> • Nerve supply of trachea is from Vagi and recurrent laryngeal nerves. • Sympathetic nerves supply the Trachealis muscle.
Tracheal deviation	<ul style="list-style-type: none"> • Ipsilateral: Collapse and fibrosis, Spontaneous Pneumothorax • Contralateral: Tension Pneumothorax
Tracheostomy	<ul style="list-style-type: none"> ➤ Tracheostomy decreases dead space by 30-50% ➤ The ideal site for Tracheostomy in adults : C2-C3 tracheal rings ➤ For children : C3-C4 -- tracheal rings. ➤ Prefer C3 > C4 for Children, while C2 > C3 for adults. ➤ The most common nerve damage during tracheostomy is recurrent laryngeal nerve. ➤ Most common vein damage during Tracheostomy is inferior thyroid vein. ➤ The most common cause of heavy bleeding during Tracheostomy anterior jugular vein & Isthmus of thyroid. ➤ In Children during tracheostomy : risk of damage to Left Brachiocephalic vein & Rt Brachiocephalic trunk or innominate artery ➤ During Tracheostomy one should not injure 1st tracheal ring ➤ During Tracheostomy heat loss by evaporation ➤ Tracheostomy is of no benefits if the lesion is at the level of the carina
LUNGS	<ul style="list-style-type: none"> ➤ The right lung is normally a little larger than the left lung because the middle mediastinum, Containing the heart, bulges more to the left than to the right. ➤ The pulmonary arteries deliver deoxygenated blood to the lungs from the right ventricle of the Heart. ➤ Oxygenated blood returns to the left atrium via the pulmonary veins. ➤ Pulmonary veins are the major venous drainage of lungs ➤ Pulmonary varix is dilatation of Left pulmonary vein and drains into Left atrium. ➤ Right Lung has three lobes and two Fissures. Normally, the lobes are freely Movable against each other because they are separated to hilum by Invaginations of visceral pleura. These Invaginations form the fissures:

	<ul style="list-style-type: none">▪ oblique fissure separates the inferior Lobe (lower lobe) from the superior lobe and the middle lobe of the right lung▪ Horizontal fissure separates the Superior lobe (upper lobe) from the Middle lobe Left Lung Has two lobes separated by an Oblique fissure. The oblique fissure of the Left lung is slightly more oblique than the Corresponding fissure of the right lung As with the right lung, the orientation of the oblique fissure determines where to Listen for lung sounds from each lobe		
Relations of Lungs (IMP)	<ul style="list-style-type: none">• Arch of aorta arches arch over the left lung.• Azygos vein arches over the right lung• Phrenic nerve anterior to the root of both lungs• Vagus nerve : posterior to the root of both lungs• Loops around the aortic arch behind the Ligamentum arteriosum is Left RLN• Hooks around the right subclavian artery : Right recurrent laryngeal nerve• Both right and left recurrent laryngeal nerve Pass in the groove between esophagus and trachea. Aortic arch winds around left bronchus.• Structure not compressed in aortic aneurysm is Phrenic nerve• Lower respiratory components sympathetic T2-T4		
Right and Left Lung Structures	Right Lung Superior to inferior	Left Lung Superior to inferior (ABV)	Both Lungs Anterior to Posterior (VAB)
	1. Eparterial bronchus	Pulmonary artery	Pulmonary Vein
	2. Pulmonary artery	Principle bronchus	Pulmonary artery
	3. Hyparterial bronchus	Pulmonary Veins	A bronchus Left main bronchus on Left side, Eparterial & Hyparterial on Right.
	4. Pulmonary Vein		
NOTE	<ul style="list-style-type: none">○ The pulmonary artery is superior at the hilum, the pulmonary veins are inferior, and the bronchi are somewhat posterior in position.○ The difference in the arrangement of structures from above downwards on the 2 sides is because:<ul style="list-style-type: none">• Right main bronchus before going into the lung at hilum splits into 2 lobar bronchi, the upper Lobar bronchus enters above the pulmonary artery (Eparterial bronchus) while lower lobar Bronchus enters below the pulmonary artery (Hyparterial bronchus).		
Pulmonary ligament	A thin blade-like fold of pleura projects inferiorly from the root of the lung and extends from the Hilum to the mediastinum. It may stabilize the position of the inferior lobe and may also accommodate the down-and-up translocation of structures in the root during breathing.		
FUNCTIONAL CLASSIFICATION OF RESPIRATORY SYSTEM			
Between the trachea and the alveolar sacs -- the airways divide 23 times.			
<ul style="list-style-type: none">• These multiple divisions greatly increase the total cross-sectional area of the airways, from 2.5 cm in the trachea to 11,800 cm in the alveoli. . The velocity of airflow in the small airways Declines to very low values.• The arrangement of Air ways is as follows. Trachea → Major/Primary bronchi → 2° bronchi → Segmental /3° bronchi → Terminal bronchioles → Respiratory bronchioles → Alveolar duct → alveolar sac → alveoli.			
Conducting Zone	<ul style="list-style-type: none">○ 16 divisions from Nasal cavity → pharynx → Larynx → Trachea → Bronchi and Bronchioles○ Terminal bronchioles signifies the end of the conduction zone .They Contain Clara cells which are Reserve cells Producing little surfactant .○ Clara Cells are Present in Terminal bronchioles.○ Goblet Cells are present in Tertiary bronchus / bronchi.○ Terminal Bronchioles are Lined by Simple cuboidal epithelium No mucinous cell / goblet cell/ cartilage○ Absence of cartilage in terminal bronchioles differentiates it from conducting Zone which has cartilage (e.g., trachea)		

	<ul style="list-style-type: none"> Function of conducting zone from Nose to terminal bronchioles is Air conditioning , to warm, humidify/moisturize the air Conducting zone doesn't take part in gaseous exchange , hence called Anatomical dead space -- it is 150ml approx.
Respiratory Zone	<ul style="list-style-type: none"> 7 divisions from Respiratory Bronchioles → Alveolar sacs → Alveoli Gaseous exchange occurs here. Respiratory Bronchioles are Lined by Simple Cuboidal epithelium or low columnar epithelium, Diameter—0.5mm, Absent Goblet cell , Gland, and Cartilage Alveoli: There are 300 million alveoli in each lung. Alveoli surface is dry due to negative interstitial fluid pressure. Alveoli is the smallest unit ; lined by Simple Squamous epithelium for gas exchange. Alveolar ducts are Lined by simple squamous epithelium > simple cuboidal. The ducts are Bounded entirely by alveoli, the alveoli protruded from their lumens and their openings are Separated by a very small segments or knobs of smooth muscles. Alveolar sac: Each has main alveoli opening into its lumen and without any wall/muscles between their openings. Ground substance of Alveoli = Basement membrane Ground substance of Alveolar ducts = Alveoli The pulmonary endothelium selectively takes up norepinephrine and serotonin (5HT) from blood While his results in the removal of 30% of Norepinephrine and 98% of serotonin (5HT) in a single pass through the lungs.
Blood-Air Barrier	<p>Through this structure gas exchange take place Respiratory membrane -- Blood-Air Barrier consist of :</p> <ol style="list-style-type: none"> Simple squamous cell (Type 1 Pneumocytes) Common Basal lamina Endothelial cell (simple squamous)



Left Main/ Principal Bronchus	Right Main/ Principal Bronchus
<ul style="list-style-type: none"> Narrow , Longer , Horizontal 2inch or 5cm. Two lobes : Superior and inferior lobar bronchus left main bronchus on entering the hilum divides into; <ol style="list-style-type: none"> Superior Lobar bronchus Inferior Lobar bronchus 	<ul style="list-style-type: none"> Wider , Shorter , Vertical , 1inch/2.5 cm. foreign body mostly lodges on right side. Three Lobes <ol style="list-style-type: none"> Superior lobar bronchus: from Right main bronchus before entering the hilum. Middle & inferior : from Right main bronchus on entering hilum. <p>Eparterial bronchus (right superior Lobar bronchus) is a branch of the right Main bronchus given off about 2.5 cm from the bifurcation of the trachea. This Branch supplies the superior lobe of the Right lung and is the most superior of all Secondary bronchi. It arises above the Level of the pulmonary artery, and for This reason is named the Eparterial Bronchus.</p> <p>Hyparterial bronchus : All other distributions falling below Pulmonary artery are Termed Hyparterial</p>



Defense Mechanism of Respiratory System

- The hairs in the Nostrils strain out many particles larger than 10 μm in diameter.
- Particles 2 to 10 μm in diameter generally fall on the walls of the bronchi can initiate reflex bronchial constriction and coughing. Alternatively, they can be moved away from the lungs by the "mucociliary escalator."
- Cilia Typically beat at rates of 10 15 Hz. The ciliary mechanism can move Particles away from the lungs at a rate of at least 16 mm/min.
- When ciliary motility is defective, as can occur from smoking, other environmental conditions, or genetic deficiency, mucus transport is virtually absent. This can lead to chronic sinusitis, recurrent Lung infections, and bronchiectasis.
- Alveolar macrophages = Dust cells

ZONES OF LUNGS

ZONE 1 (Area of zero flow)	ZONE 2 (Area of intermittent flow)	ZONE 3 (Area of Continuous flow)
<ul style="list-style-type: none"> When alveolar pressure is greater than pulmonary capillaries pressure, capillaries remain Collapsed and there is no blood flow. it does not occur in normal lungs. It occurs following hemorrhage or while blowing on a musical Instrument 	<ul style="list-style-type: none"> Pulmonary capillaries collapse during diastole (zero blood flow) and open during systole (full blood flow). So, blood flow is intermittent. It occurs in normal lungs in Standing position. 	<ul style="list-style-type: none"> When pulmonary capillary pressure is greater than alveolar pressure, capillaries always remain Opened and there is continuous blood flow. It occurs in the normal lung in Standing/ Laying position & Exercise

BRONCHOPULMONARY SEGMENTS

- They are the anatomic, functional, and surgical unit of lungs.
- They have own blood supply, lymphatics, and, autonomic supply .
- All are Aerated by Tertiary bronchus.
- There are 10 Bronchopulmonary segments in the right lung and 10 in the left lung.
- Left second is absent at birth. Medial basal is the 7th segment

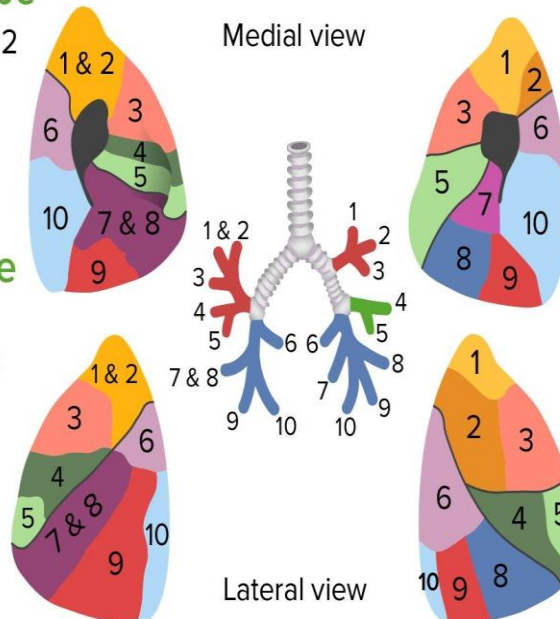
Right lung	$3 + 2 + 5 = 10$ <ul style="list-style-type: none"> Superior lobe: 3 → Apical, Posterior ,Anterior Middle lobe: 2 → Lateral, Medial Inferior lobe: 5 → Superior(Apical), Medial Basal, Anterior basal, Lateral basal, Posterior Basal
Left lung	$5 + 5 = 10$ <ul style="list-style-type: none"> Superior lobe → Apical, Posterior, Anterior, Superior lingular, Inferior lingular. Inferior lobe → Superior(apical), Medial basal, Anterior basal, Lateral basal, Posterior Basal

Left superior lobe

- Apical posterior 1 & 2
- Anterior 3
- Superior lingula 4
- Inferior lingula 5

Left inferior lobe

- Superior 6
- Anterior basal 7 & 8
- Lateral basal 9
- Posterior basal 10



Right superior lobe

- Apical 1
- Posterior 2
- Anterior 3

Right middle lobe

- Lateral 4
- Medial 5

Right inferior lobe

- Superior 6
- Medial basal 7
- Anterior basal 8
- Lateral basal 9
- Posterior basal 10

MEDIASTINUM

- The mediastinum is divided into superior and inferior mediastinum by an imaginary plane passing from the sternal angle anteriorly to the lower border of the body of the 4th thoracic vertebra posteriorly.
- The inferior mediastinum is further subdivided into the middle mediastinum, anterior Mediastinum, and posterior mediastinum: Details of all are given below.

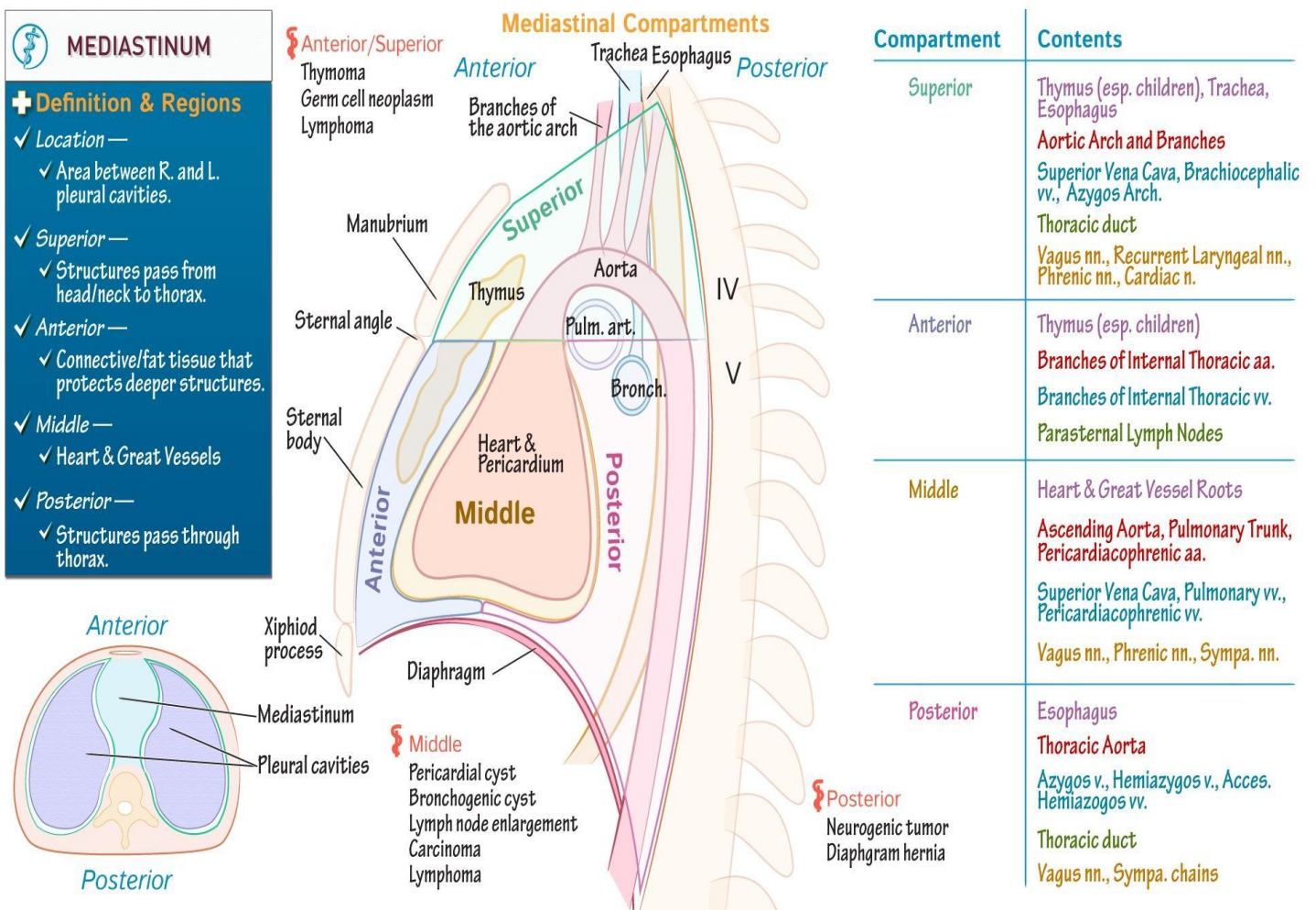
Superior Mediastinum	<ul style="list-style-type: none"> ○ It is posterior to the manubrium of the sternum and anterior to the Bodies of the first four thoracic vertebrae. ○ Superior boundary is an oblique plane passing from the jugular notch upward and posteriorly to the superior border of vertebra T1. ○ Inferiorly, a transverse plane passing from the sternal angle to the intervertebral disc between Vertebrae T4/T5 separates it from the inferior mediastinum. ○ Laterally, it is bordered by the Mediastinal part of the parietal pleura on either side. ○ The superior mediastinum is continuous with the neck superiorly and with the inferior Mediastinum inferiorly. ○ The major structures found in the superior mediastinum include Thymus, Right and left brachiocephalic veins, Superior vena cava, Arch of the aorta- with its 3 large branches, Vagus nerves, Trachea, Esophagus, Phrenic nerves, Left recurrent laryngeal branch of the left vagus nerve Thoracic duct. ○ Infection of the pre-vertebral fascia can spread to Superior Mediastinum, anterior to Vertebrae. ○ Arch of aorta is in Superior Mediastinum (frequently asked in exams)
Middle Mediastinum	<ul style="list-style-type: none"> ○ centrally located in the thoracic cavity ○ contains the pericardium, heart, origins of the great vessels, various nerves, and smaller vessels. ○ Cysts are most found in the middle mediastinum.
Anterior Mediastinum	<ul style="list-style-type: none"> ○ The major structure in the anterior mediastinum is a portion of the thymus, Mediastinal branches of the internal thoracic vessels, and Sternopericardial ligaments, which pass from the posterior surface of the body of the sternum to the fibrous pericardium. ○ Infection from Pretracheal fascia can spread into the anterior mediastinum. ○ IMP Structure is Thymus (commonly asked in exams) ○ The most common tumour of the anterior mediastinum is Thymoma
Posterior Mediastinum	<ul style="list-style-type: none"> ○ The posterior mediastinum is posterior to the pericardial sac and diaphragm and anterior to the Bodies of the mid and lower thoracic vertebrae ○ Superior boundary is a transverse plane passing from the sternal angle to the Intervertebral Disc between vertebra T4/T5 ○ inferior boundary is the diaphragm. ○ Laterally, it is bordered by the Mediastinal part of parietal pleura on either side. ○ Superiorly, it is continuous with the superior mediastinum. ○ Major structures in the posterior mediastinum include DATES. <ul style="list-style-type: none"> • Descending aorta and their 9 post intercostal branches • Azygos and hemiazygos vein • Thoracic duct - found in both superior and posterior mediastinum. • Esophagus and Sympathetic trunk/ganglia • Tumors especially of neurogenic origin are seen in Posterior Mediastinum. <p style="text-align: center;"><u>TUMORS</u></p> <ul style="list-style-type: none"> • The most common tumor in the posterior mediastinum is Neurogenic tumor. • Most common Mediastinal mass is Neurogenic tumor. • Most common Mediastinal mass in children is Neurogenic tumor in posterior Mediastinum. • Most common malignant mass of mediastinum is lymphoma. • Most common anterior Mediastinal mass is Thymoma


THYMUS

- **Located In anterior mediastinum** , Bilobed, lobulated, and, Larger in children.
- Plays a major role in development of immune system.
- Blood supply: Internal thoracic artery
- Venous drainage: Thymic to left brachiocephalic & some to internal thoracic vein.
- Embryology: **Endoderm(epithelium) derived from ventral 3rd pharyngeal Pouch** (+/- ventral recess 4th pouch). Lymphocytes from mesenchyme source
- Thymus extends from lower part of Neck through Superior into Anterior Mediastinum
- Attains greatest size in neonate, continues to Grow, involute after Puberty.
- Most Prominent in Children , from 4th Costal cartilage to lower pole of Thyroid Gland
- **Thymus promotes T-cell differentiation & Maturation (Cell Mediated Immunity)**
- Thymus produce Thymosin for T-cell Maturation.

Relations:

- **Anterior** : Sternothyroid & Sternohyoid muscle, Manubriosternum + upper body of Sternum + adjacent costal cartilage
- **Posterior** : Trachea , Pericardium, Arch of Aorta and Left brachiocephalic Vein.



ROLE OF RESPIRATORY MUSCLES IN BREATHING	
Inspiration	<ul style="list-style-type: none"> 2 cycle, active process Quite breathing is by Diaphragm. Normal breathing takes 3-5 % Energy expenditure of the body. Diaphragm: Most Powerful and major inspiratory muscle Contraction of diaphragm increase in vertical thoracic diameter. Increase Lung capacity by 2/3rd. Exercise : External intercostal muscle Increase the transverse diameter by elevation of ribs A man with RTA having multiple rib fracture and his abdomen is moving with Breathing, the muscle which involved is : External Oblique > Rectus abdominus > external intercostal muscle. Accessory muscle SCM -- Elevate sternum and Scalenus group -- Elevate upper ribs
Expiration	<ul style="list-style-type: none"> 3 cycles , under resting condition expiration is normally a passive Quite breathing. Normal quite expiration is brought about by contraction/recoil of Elastic tissue in Thoracic and lung wall. A major part of energy (70% of the work of breathing) is utilized during breathing to overcome elastic recoil of lungs. Exercise Internal intercostal muscle (pull ribs downward and inward) Abdominal muscle: Rectus abdominis (main muscle) Transverses abdominis, Internal and external oblique muscle Elastic Recoil of the lung is a tendency to return to its original shape. Recoil, as a force, always acts to collapse the lung. Almost 70% of work of breathing to overcome the elastic recoil of lungs. Surfactant account for 70 % of the elastic recoil
Work of Breathing	<ul style="list-style-type: none"> The amount energy required to ventilate the lung and overcome Resistance. Work of breathing Pressure x Volume
Summary	<p>Muscles of:</p> <ul style="list-style-type: none"> Quite inspiration → Diaphragm & External ICM -- in both Quite & forceful inspiration Forced inspiration → SCM , Scalene muscles , serratus anterior. Quite Expiration → passive process; by elastic recoil of Lungs Forced Expiration: internal ICM. Accessory muscles of Expiration: Abdominal muscles (Rectus abdominus > external Oblique) After RTA : difficulty in Breathing → damage to Diaphragm After RTA : difficulty in Breathing + abdomen is moving out with breathing : External Oblique damaged. Vertical diameter: Increases by diaphragm. Transverse diameter inc by Bucket handling movement via External ICM Anteroposterior diameter inc by Pump Handle movement by Ext ICM Sternum moves Upward & Forward in Pump handle movement →  AP diameter.

DIAPHRAGM	
Attachments	<ul style="list-style-type: none"> A thin musculotendinous structure that fills the inferior thoracic aperture and separates the thoracic cavity from the abdominal cavity. Develops from septum transversum in 8-12th wk. It is attached peripherally to <ul style="list-style-type: none"> xiphoid process, costal margin of thoracic wall, ends of ribs XI and XII Ligaments across posterior abdominal wall, and, lumbar vertebrae.
Relations	<ul style="list-style-type: none"> Right dome reaches 4th costal space (nipple) in expiration. Left dome reaches 5th rib in expiration. Superiorly – pericardium, basal lung segments Inferiorly – on Right → liver, suprarenal, kidney, while on Left → stomach, suprarenal, kidney & spleen Posteriorly – Aorta, Azygos veins, oesophagus, Vagus nerve, and, pleural folds.

	<ul style="list-style-type: none"> Anterior Hiatus at T9: Superior epigastric vessels pass through it. From Crura passes the: Greater, Lesser & Least splanchnic nerves. Behind medial Arcuate ligament: Sympathetic chain Behind lateral Arcuate ligament: Subcostal (T12) nerve. 						
Openings & their contents (IMP)	<ul style="list-style-type: none"> Three openings in diaphragms through which structures pass. These are arranged Anterior to Posterior. Aortic Opening is the posterior most. <table border="1"> <tr> <td>Vena caval Opening (T8)</td><td>T8 level (8 letters of Vena cava. It contains (Mnemonics – VIP) → Inferior vena cava, Right Phrenic nerve.</td></tr> <tr> <td>Oesophageal Opening (T10)</td><td>At T10 level -- 10 letters of Esophagus. It contains (Mnemonics → Phagus – vagus). Esophagus, Both Vagal trunks, and, branches of Left gastric artery.</td></tr> <tr> <td>Aortic Opening (T12)</td><td>Aortic opening has 12 letters. So, it is at T12 level. It contains (Mnemonics -- AAT) Aorta, Azygos vein, Thoracic duct pass through it.</td></tr> </table>	Vena caval Opening (T8)	T8 level (8 letters of Vena cava. It contains (Mnemonics – VIP) → Inferior vena cava, Right Phrenic nerve.	Oesophageal Opening (T10)	At T10 level -- 10 letters of Esophagus. It contains (Mnemonics → Phagus – vagus). Esophagus, Both Vagal trunks, and, branches of Left gastric artery.	Aortic Opening (T12)	Aortic opening has 12 letters. So, it is at T12 level. It contains (Mnemonics -- AAT) Aorta, Azygos vein, Thoracic duct pass through it.
Vena caval Opening (T8)	T8 level (8 letters of Vena cava. It contains (Mnemonics – VIP) → Inferior vena cava, Right Phrenic nerve.						
Oesophageal Opening (T10)	At T10 level -- 10 letters of Esophagus. It contains (Mnemonics → Phagus – vagus). Esophagus, Both Vagal trunks, and, branches of Left gastric artery.						
Aortic Opening (T12)	Aortic opening has 12 letters. So, it is at T12 level. It contains (Mnemonics -- AAT) Aorta, Azygos vein, Thoracic duct pass through it.						
Neurovasculature	<ul style="list-style-type: none"> Arteries -- Intercostal, Musculophrenic, phrenic, pericardiophrenic, superior phrenic. The veins drain into the brachiocephalic, Azygos veins or Abdominal veins (left suprarenal vein and inferior vena cava) Innervation: Motor: Right and left Phrenic nerves-(C3,4,5)--(C4 = largest contribution) Sensory: The parietal pleura and the peritoneum covering the central surface of the diaphragm are from phrenic nerve The Periphery of the diaphragm from lower six intercostal nerve. 						
Abnormalities	<p><u>Congenital diaphragmatic hernia:</u></p> <ul style="list-style-type: none"> CDH caused by the incomplete pleuro-peritoneal membranes > failure of the pleuroperitoneal membrane to develop or fuse with the other compartments of the diaphragm. Respiratory difficulty is the key presentation with an empty feeling of the abdomen as the abdominal contents move towards chest. Bochdalek hernia is the most common type of (CDH) Also known as a postero-lateral diaphragmatic hernia. Morgagni hernia, known as anterior diaphragmatic hernia, is on the right anterior side. It is characterized by herniation through the foramina of Morgagni, and, it is associated with lung hypoplasia. Diaphragmatic eventration: Upward displacement of abdominal contents secondary to a congenitally thin hypoplastic Diaphragm due to incomplete muscularization of the diaphragm, complete almost always on the left side while partial is common on the right side 						

FOREIGN BODY	
Supine position	Apical/superior segment of right lower Lobe. (segment 6)
Sitting or standing	Posterior- Basal segment of right lower lobe (segment 10)
Lying on Right	Posterior bronchopulmonary segment of right upper lobe (segment 02)
Lying on Left	Inferior Lingular segment of left upper lobe (segment 05)

- In Short: For Supine, Sitting/Standing: Rt Lower Lobes. For Left / Right sides: Upper Lobes bronchus.

Key Facts

- Tumor/foreign body in superior lobar bronchus will affect apical superior Bronchopulmonary Segment.
- Secondary Tuberculosis: involve Apical and posterior segment of upper lobes because of high V/Q ratio
- Primary Tb involve mid/lower lobe
- A child presented with Dyspnea, choking, on X-ray foreign body on Left Lobe bronchus: Cause is situs inversus.
- Aneurysm of Arch of Aorta will compress Left Upper lobe bronchus.
- In Midaxillary line all three lobes of lung can be auscultated
- in sitting position, resonance of the lungs can be auscultation from back of the chest till 10th Rib**
- For back of chest -- 10th rib; lateral sides -- 8th rib; Front of chest -- 6th rib**

- ✚ For Pericardiocentesis Sub costal approach is the best option or A needle is inserted into the pericardial cavity through the fifth intercostal space left to the Sternum
- ✚ Hyper-resonance area is Right mid-clavicular line in T2-T4 level
- ✚ 2nd to 4th intercostal space on the right is The Area normally resonant to percussion:
- ✚ Nipple is at 4th ICS, 10cm from the midline, T4 – dermatomal level. Oblique fissure of lung is at T3-T6
- ✚ **Pulmonary Vein Varix** is an anomalous dilatation of the pulmonary vein, with no evidence of increased venous pressure, which fills at the same rate as the Normal pulmonary veins and **drains into the left atrium** with delay compared to other Normal pulmonary veins
- ✚ Piriform Fossa is Also called smuggler's fossa (foreign body may lodge here e.g., Fish bone.)
- ✚ Piriform sinus tumors account for 70% of cancer that originates in the hypopharynx
- ✚ Covered by mucous membrane. Beneath the membrane run the internal laryngeal nerve
- ✚ Thing that can be seen first on bronchoscopy is right upper lobe
- ✚ Aspiration of fluid during fits can be prevented by closure of false vocal cord.
- ✚ The Right lung is larger than the left lung and is divided by oblique fissure and horizontal fissure into three lobes.
- ✚ The left lung is divided by oblique fissure into two lobes upper and lower lobes.
- ✚ There is no horizontal fissure in the left lung.
- ✚ Large particles become deposited in the mucus layer that lies within the bronchi.
- ✚ Apex of lung reaches 2.5cm above medial one third of the clavicle.

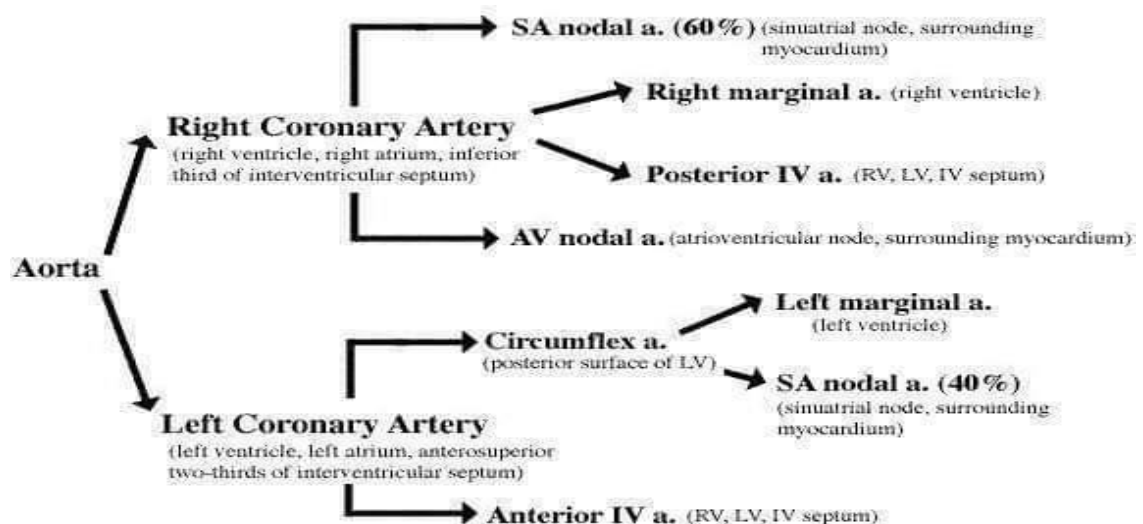
DERMATOMES

- T3-anterior and posteriorly extends at the level of the lower axilla
- **T4- anteriorly at the level of the nipple**
- T5 – anteriorly at the level just inferior to the nipple
- T6-T7 -anteriorly at the level of the xiphoid process
- T7-T9 -evenly distributed anteriorly between T6 and T10 dermatomes
- **T10-anteriorly at the level of the umbilicus**
- T11- evenly distributed anteriorly between T10 and T12 dermatomes
- T12 – anteriorly just superior to the pelvic girdle

ANATOMY OF THE HEART

Borders of Heart	<ul style="list-style-type: none"> ○ The right border is formed by the right atrium. ○ ON X-ray Rt border formed by SVC + Rt Atrium > SVC > Rt Atrium ○ The left border is mainly formed by the left ventricle. ○ The apex is the tip of the left ventricle. And is found in the left fifth Intercostal space. ○ The superior border is formed by right and left auricles plus conus arteriosus of right ventricle. ○ The inferior border is formed at the diaphragm, mostly by the right Ventricle > Lt Ventricle ○ RV is the most injured in trauma as it is anterior most part of heart. ○ LA is the most posterior part of heart. ○ LA enlargement can compress esophagus leading to dysphagia.
Surfaces of Heart	<ul style="list-style-type: none"> ○ The anterior (sternocostal) surface is formed primarily by the right Ventricle. ○ The posterior surface/ base is formed primarily by the left atrium. ○ The Inferior/diaphragmatic surface is formed primarily by the left ventricle > Rt Ventricle ○ Rt Pulmonary surface formed by Rt Atrium ○ Lt Pulmonary surface/Cardiac impression by Left Ventricle
Venous Drainage	<ul style="list-style-type: none"> ○ The major cardiac veins draining the heart course in the sulci and accompany the arteries but do not carry the same names. The major veins Are the following: Coronary sinus: The main vein of the coronary circulation; it lies in the posterior coronary sulcus. It drains to an opening in the right Atrium. ○ It Drains 2/3rd of Heart and develops from the left sinus venosus. Great cardiac vein lies in the anterior interventricular sulcus with The LAD artery. ○ It is the main tributary of the coronary sinus.

	<p>Middle cardiac vein lies in the posterior interventricular sulcus with the posterior interventricular artery. It joins the coronary sinus.</p> <ul style="list-style-type: none"> ○ Venae cordis minimae (thebesian veins) and anterior cardiac veins ○ The venae cordis minimae and anterior cardiac veins open directly to heart chambers 				
Blood supply	<p>Right Coronary and Left Coronary artery – both are branches of ascending aorta.</p> <ul style="list-style-type: none"> ○ Dominance is determined by the artery giving Posterior Inter ventricular artery. ○ Mostly RCA gives posterior descending/Posterior Inter ventricular artery → Right Dominance in 85 % of cases. ○ If PDA is given by LCX is called Left dominant supply (8%) ○ If PDA is given by both RCA & LCX than it is called Co-Dominant Circulation (7 %) ○ Main Blood supply to Heart is LAD ○ Both RCA & LCA may have : Marginal, SA nodal and Posterior IVA. 				
<table border="1"> <thead> <tr> <th>RIGHT CORONARY ARTERY</th><th>LEFT CORONARY ARTERY</th></tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • It arises from anterior aortic sinus (Right Aortic sinus) • Goes vertically to cross inferior border of heart to continue posteriorly & anastomose with LCA • Supplies RA + RV & Parts of LA , LV , skips Left Atrium • Supplies whole conducting system of Heart except RBB. • So , SA Node , AV node, Bundle of His / AV bundle and LBB are all supplied by RCA • RBB supplied by LCA • LBB supplied by both RCA + LCA. <p>Branches:</p> <ol style="list-style-type: none"> 1. SA nodal artery – supplies 60 % SA node. 2. AV nodal artery – supplies AV node 3. Rt Marginal artery supplies Apex of Heart + Rt Ventricle. 4. Posterior Interventricular / Post Descending artery in 85% of cases given by RCA. Supplies Posterior 1/3rd of Interventricular septum + both Ventricles. </td><td> <ul style="list-style-type: none"> • Arises from Left Aortic Sinus • Supplies LA, LV, RV, Apex , Bundle of HIS, RBB, LBB • Skips Right Atrium (not supplied by LCA) • Bundle of HIS : RCA > LAD. • LCA gives two main branches → LCX + LAD and • other branches are Posterior IVA, SA Nodal (40%) , Left Marginal artery. <p>Branches</p> <p>Left Anterior Descending or Anterior Interventricular Artery Main artery supplying the Heart. LAD supplies Ant surface of both ventricles , Ant 2/3 of IV septum , Anterolateral Papillary Muscle Apex of Heart supplied by LAD > Rt Marginal artery.</p> <p>Left Circumflex Artery LCX supplies Lateral and Posterior wall of Left Ventricle , Anterolateral Papillary Muscle. Supplies Both LA & LV In circumferential infarct involving Lateral / posterior Left ventricle, LCX is involved.</p> <p>Posterior Descending /Posterior Interventricular Artery: PDA supplies Post 1/3 of IVS, Post walls of ventricles, Posteromedial Papillary Muscle.</p> </td></tr> </tbody> </table>		RIGHT CORONARY ARTERY	LEFT CORONARY ARTERY	<ul style="list-style-type: none"> • It arises from anterior aortic sinus (Right Aortic sinus) • Goes vertically to cross inferior border of heart to continue posteriorly & anastomose with LCA • Supplies RA + RV & Parts of LA , LV , skips Left Atrium • Supplies whole conducting system of Heart except RBB. • So , SA Node , AV node, Bundle of His / AV bundle and LBB are all supplied by RCA • RBB supplied by LCA • LBB supplied by both RCA + LCA. <p>Branches:</p> <ol style="list-style-type: none"> 1. SA nodal artery – supplies 60 % SA node. 2. AV nodal artery – supplies AV node 3. Rt Marginal artery supplies Apex of Heart + Rt Ventricle. 4. Posterior Interventricular / Post Descending artery in 85% of cases given by RCA. Supplies Posterior 1/3rd of Interventricular septum + both Ventricles. 	<ul style="list-style-type: none"> • Arises from Left Aortic Sinus • Supplies LA, LV, RV, Apex , Bundle of HIS, RBB, LBB • Skips Right Atrium (not supplied by LCA) • Bundle of HIS : RCA > LAD. • LCA gives two main branches → LCX + LAD and • other branches are Posterior IVA, SA Nodal (40%) , Left Marginal artery. <p>Branches</p> <p>Left Anterior Descending or Anterior Interventricular Artery Main artery supplying the Heart. LAD supplies Ant surface of both ventricles , Ant 2/3 of IV septum , Anterolateral Papillary Muscle Apex of Heart supplied by LAD > Rt Marginal artery.</p> <p>Left Circumflex Artery LCX supplies Lateral and Posterior wall of Left Ventricle , Anterolateral Papillary Muscle. Supplies Both LA & LV In circumferential infarct involving Lateral / posterior Left ventricle, LCX is involved.</p> <p>Posterior Descending /Posterior Interventricular Artery: PDA supplies Post 1/3 of IVS, Post walls of ventricles, Posteromedial Papillary Muscle.</p>
RIGHT CORONARY ARTERY	LEFT CORONARY ARTERY				
<ul style="list-style-type: none"> • It arises from anterior aortic sinus (Right Aortic sinus) • Goes vertically to cross inferior border of heart to continue posteriorly & anastomose with LCA • Supplies RA + RV & Parts of LA , LV , skips Left Atrium • Supplies whole conducting system of Heart except RBB. • So , SA Node , AV node, Bundle of His / AV bundle and LBB are all supplied by RCA • RBB supplied by LCA • LBB supplied by both RCA + LCA. <p>Branches:</p> <ol style="list-style-type: none"> 1. SA nodal artery – supplies 60 % SA node. 2. AV nodal artery – supplies AV node 3. Rt Marginal artery supplies Apex of Heart + Rt Ventricle. 4. Posterior Interventricular / Post Descending artery in 85% of cases given by RCA. Supplies Posterior 1/3rd of Interventricular septum + both Ventricles. 	<ul style="list-style-type: none"> • Arises from Left Aortic Sinus • Supplies LA, LV, RV, Apex , Bundle of HIS, RBB, LBB • Skips Right Atrium (not supplied by LCA) • Bundle of HIS : RCA > LAD. • LCA gives two main branches → LCX + LAD and • other branches are Posterior IVA, SA Nodal (40%) , Left Marginal artery. <p>Branches</p> <p>Left Anterior Descending or Anterior Interventricular Artery Main artery supplying the Heart. LAD supplies Ant surface of both ventricles , Ant 2/3 of IV septum , Anterolateral Papillary Muscle Apex of Heart supplied by LAD > Rt Marginal artery.</p> <p>Left Circumflex Artery LCX supplies Lateral and Posterior wall of Left Ventricle , Anterolateral Papillary Muscle. Supplies Both LA & LV In circumferential infarct involving Lateral / posterior Left ventricle, LCX is involved.</p> <p>Posterior Descending /Posterior Interventricular Artery: PDA supplies Post 1/3 of IVS, Post walls of ventricles, Posteromedial Papillary Muscle.</p>				



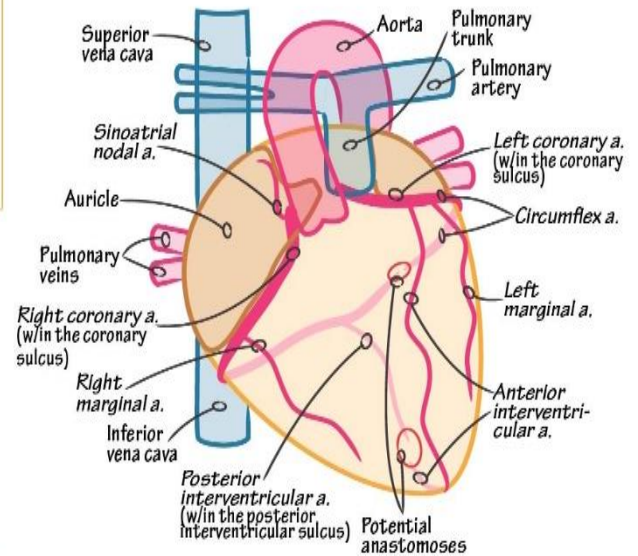
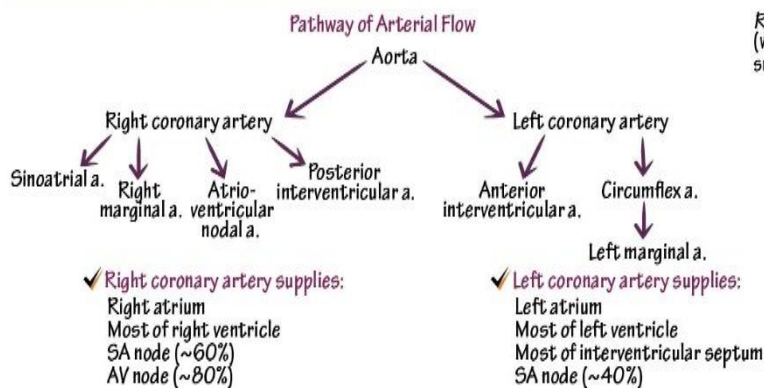
CORONARY ARTERIES

Clinical Correlations

- ✓ No redundancy in coronary vasculature — Occlusion of vessels causes ischemia and myocardial infarction.
- ✓ Treatment for coronary artery occlusion includes:
 - ✓ Coronary angioplasty — Widen artery at site of obstruction.
 - ✓ Coronary artery bypass graft — Graft vascular segments to circumvent obstructed regions of coronary arteries.

Common Coronary Artery Branch Patterns:

- ✓ **Right dominant** — RCA gives rise to posterior interventricular a. (most common)
- ✓ **Left dominant** — LCA gives rise to posterior interventricular a. (less common)
- ✓ **Codominance** — RCA and LCA contribute to posterior interventricular a.



CLINICAL CORRELATIONS

In Myocardial Infarction --- LCA > RCA > LCX involved

- LAD Obstruction in 50% cases
- RCA Obstruction in 30% cases
- LCX occluded in 20% cases.

Great cardiac vein runs with anterior interventricular artery or LAD

Middle cardiac vein runs with posterior interventricular artery

Small cardiac vein runs with right marginal artery

Coronary sinus runs with LCX

- Coronary Artery Aneurysm – most common cause in adult Atherosclerosis
- Coronary Artery Aneurysm – most common cause in child Kawasaki
- Rheumatic heart disease is the most common cause of mitral stenosis
- Pulmonary Arterial Hypertension is the most common cause of tricuspid atresia.
- Notching from coarctation of aorta spares the 1st and 2nd Ribs
- **Most common primary cardiac tumor in children Rhabdomyoma.**
- Most common source of Cardiac metastasis = Lung Cancer (lymphoma) .
- A-Fib is most commonly associated with left atrial enlargement
- Most common cause of tricuspid insufficiency is RVH (usually from pulmonary HTN OR cor pulmonale)
- Coronary flow to LV & IVS peaks in early Diastole (Rapid filling)

PERICARDIUM

- Most common site of metastasis to the heart is pericardium.
- Supplied by Phrenic nerve mainly (P for Pericardium and phrenic)
- **Phrenic nerve is lateral to Pericardiophrenic artery.**
- Consists of 3 layers ; Outer Fibrous , inner Serous layer → (Parietal & Visceral layer.(Epicardium)
- **Visceral layer of serous pericardium is called Epicardium.**
- Pericardial space lies b/w Parietal and visceral layer, or you can say b/w Parietal layer & Epicardium.
- Fibrous pericardium is supplied by Phrenic nerve.
- Visceral pericardium is supplied by Vagus nerve / Cardiac Plexus (V For Visceral & Vagus).

HEART WALL AND PERICARDIUM

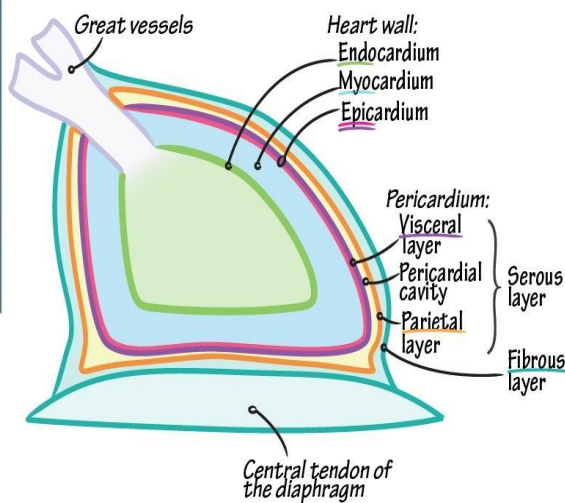
Heart Wall

- ✓ Endocardium
- ✓ Myocardium
- ✓ Epicardium

Pericardium

- ✓ Fibrous layer
- ✓ Serous layer
 - ✓ Parietal layer
 - ✓ Pericardial cavity
 - ✓ Visceral layer

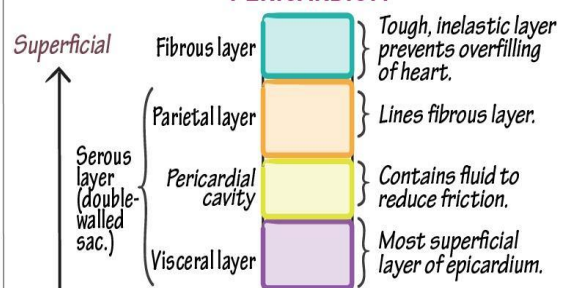
LAYERS OF THE HEART WALL AND PERICARDIUM



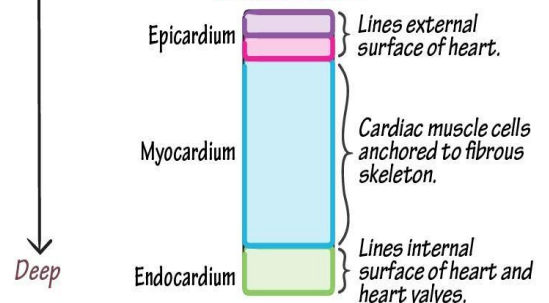
Clinical Correlations

- ✓ Endocarditis — Inflammation of endocardium disrupts blood flow.
- ✓ Myocardial infarction — Obstructed coronary flow causes cardiac muscle cell death.
- ✓ Pericarditis — Inflammation causes friction, pain, and impacts heart functioning.

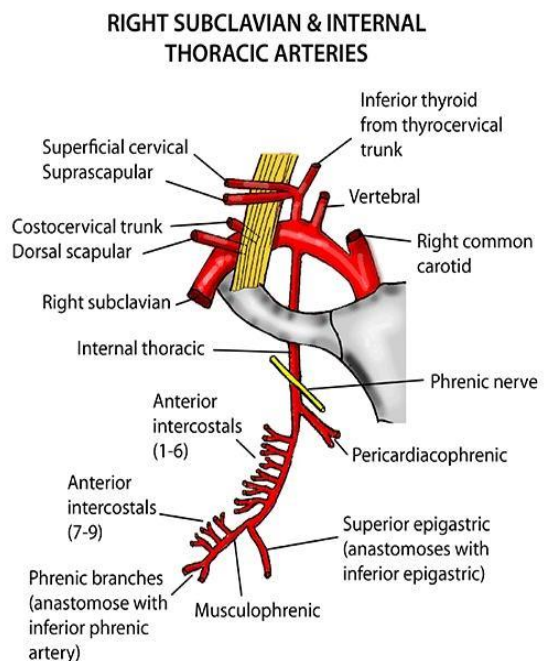
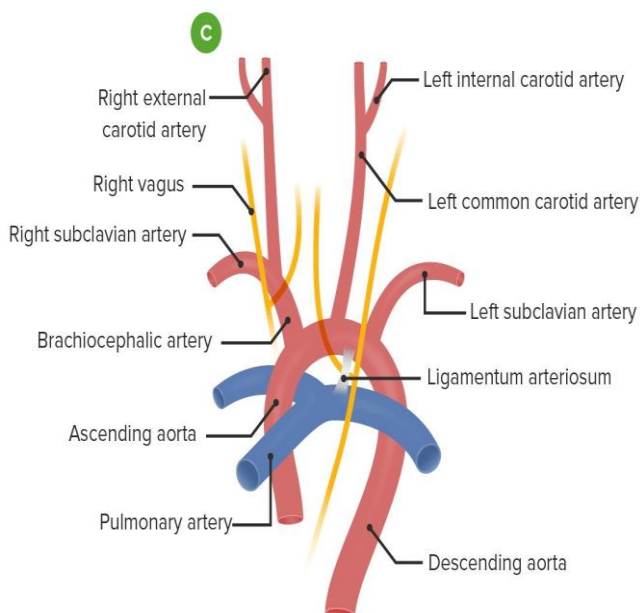
PERICARDIUM



HEART WALL



Arch of Aorta	<ol style="list-style-type: none"> 1. Brachiocephalic trunk (it gives off Right Common carotid + Rt Subclavian artery) 2. Left Common carotid artery. 3. Left Subclavian artery 						
Subclavian artery Branches	<table border="1"> <tr> <td data-bbox="451 320 587 510">1st Part</td><td data-bbox="595 320 1377 510"> Medial to Scalenus anterior , arches over Suprpleural membrane. Branches are, <ul style="list-style-type: none"> ○ Vertebral artery ○ Internal thoracic artery ○ Thyrocervical trunk → gives further inferior thyroid, Suprascapular, Transverse cervical artery) </td></tr> <tr> <td data-bbox="451 521 587 678">2nd part</td><td data-bbox="595 521 1377 678"> <ul style="list-style-type: none"> ○ Posterior to Scalenus anterior muscle ○ Costocervical artery (gives Superior Intercostal & Deep Cervical artery). ○ Dorsal scapular artery (direct branch that takes part in scapular anastomosis) </td></tr> <tr> <td data-bbox="451 689 587 739">3rd Part</td><td data-bbox="595 689 1377 739"> <ul style="list-style-type: none"> ○ Lateral to Scalene anterior ends at outer border of 1st rib ○ No branches </td></tr> </table>	1st Part	Medial to Scalenus anterior , arches over Suprpleural membrane. Branches are, <ul style="list-style-type: none"> ○ Vertebral artery ○ Internal thoracic artery ○ Thyrocervical trunk → gives further inferior thyroid, Suprascapular, Transverse cervical artery) 	2nd part	<ul style="list-style-type: none"> ○ Posterior to Scalenus anterior muscle ○ Costocervical artery (gives Superior Intercostal & Deep Cervical artery). ○ Dorsal scapular artery (direct branch that takes part in scapular anastomosis) 	3rd Part	<ul style="list-style-type: none"> ○ Lateral to Scalene anterior ends at outer border of 1st rib ○ No branches
1st Part	Medial to Scalenus anterior , arches over Suprpleural membrane. Branches are, <ul style="list-style-type: none"> ○ Vertebral artery ○ Internal thoracic artery ○ Thyrocervical trunk → gives further inferior thyroid, Suprascapular, Transverse cervical artery) 						
2nd part	<ul style="list-style-type: none"> ○ Posterior to Scalenus anterior muscle ○ Costocervical artery (gives Superior Intercostal & Deep Cervical artery). ○ Dorsal scapular artery (direct branch that takes part in scapular anastomosis) 						
3rd Part	<ul style="list-style-type: none"> ○ Lateral to Scalene anterior ends at outer border of 1st rib ○ No branches 						
Internal thoracic artery	<ul style="list-style-type: none"> • A long, paired vessel that originates from the proximal part of the subclavian artery. • It runs inferomedially and enters the thoracic cage deep to the clavicle and the first rib. • Terminating at the level of the sixth rib, it divides into two terminal branches: superior epigastric and Musculophrenic arteries. • The internal thoracic artery gives rise to numerous branches that supply the skin and muscles of the anterior aspect of the thoracic cage and the superior part of the abdominal wall. Additionally, it provides blood supply for the breasts, parietal pleura, sternum, pericardium, and thymus. <p>Branches</p> <ul style="list-style-type: none"> • Anterior collaterals: Anterior intercostal and Perforating branches, Medial mammary arteries. • Posterior collaterals : Mediastinal branches, Thymic branches , Pericardiophrenic artery, Sternal branches, Bronchial branches, and Tracheal branches • Terminal branches : Superior epigastric artery + Musculophrenic artery 						



- Subclavian artery, Brachial plexus, Thyrocervical trunk and Vagus nerve pass Posterior to anterior scalene
- Phrenic nerve and subclavian vein lie Anterior to anterior scalene.
- Anterior scalene muscle separates Subclavian vein from subclavian artery.

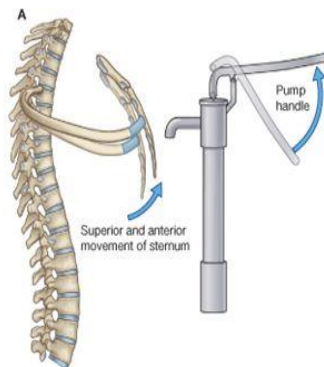
RESPIRATORY MOVEMENTS

B- MOVEMENTS OF RIBS

PUMP HANDLE MOVEMENT

Elevation of ribs

Increase in antero-posterior diameter of thoracic cavity

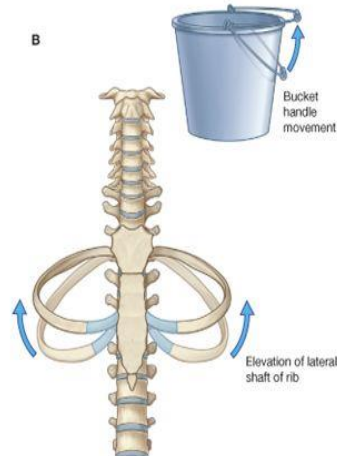


© Elsevier. Drake et al: Gray's Anatomy for Students - www.studentconsult.com

BUCKET HANDLE MOVEMENT

Elevation of ribs

Increase in lateral diameter of thoracic cavity



© Elsevier. Drake et al: Gray's Anatomy for Students - www.studentconsult.com

Esophagus

Blood Supply of Esophagus

Upper 1/3: by inferior thyroid artery

Middle 1/3: by branches from descending thoracic aorta

Lower 1/3: by branches from left gastric artery.

Veins of upper 1/3 drain into inferior thyroid veins, from middle 1/3 into azygos veins, and from lower 1/3 into left gastric vein.

Lymph Drainage of Esophagus

Upper 1/3 of esophagus drain into deep cervical nodes,

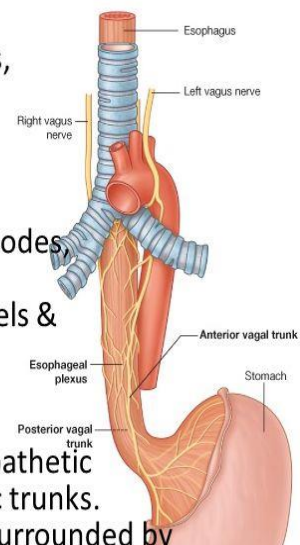
Middle 1/3 into mediastinal nodes,

Lower 1/3 into nodes along left gastric blood vessels & celiac nodes.

Nerve Supply of Esophagus

Esophagus is supplied by parasympathetic & sympathetic efferent and afferent fibers via vagi & sympathetic trunks.

In lower part of its thoracic course, esophagus is surrounded by esophageal nerve plexus.



PAST PAPERS BCQs

1. Apex of Lung involved, collapsed segment will be - Apical superior.
2. Pulmonary trunk relation with bronchus at hilum → RALS = RIGHT -- ANTERIOR , LEFT -- SUPERIOR
3. 1st posterior intercostal vein drains into : BRACHIOCEPHALIC VEIN
4. 2nd -3rd posterior intercostal veins drain into SUPERIOR INTERCOSTAL VEIN
5. 4-11th posterior intercostal veins drain into AZYGOS Vein
6. ANTERIOR Intercostal veins drain into Musculophrenic & Internal thoracic vein
7. Each intercostal space has : 2 small arteries anteriorly; 1 large artery posteriorly
8. infection of para-pharyngeal space can spread into Pre-Vertebral Fascia
9. If we ligate Thyrocervical trunk; area will still be perfused by Superior thyroid artery
10. Vagus nerve runs on right side to trachea (lateral to trachea)
11. Internal thoracic artery is behind sternum
12. In RTA , dislocation Sternoclavicular joint will lead to Trachea injury > Subclavian artery/ITA
13. Midline swelling below thyroid , no movement on tongue protrusion: Ectopic thyroid gland
14. Esophagus passes through groove of mediastinum on LEFT SIDE
15. Visceral pericardium is pain insensitive (supplied by autonomic nerves)
16. Rt Crura of diaphragm : attached to L1-L3 and their discs
17. Lt Crura of diaphragm attaches to L1/L2 and their discs
18. Right bundle branch location : SEPTO MARGINAL Trabeculae
19. LBB location : Muscular part of IVS
20. Av Bundle location : Membranous IVS
21. Level of Costodiaphragmatic recess : T10 ICS MID AXILLARY Line
22. Most prominent Esophageal constriction at PA view : ARCH OF AORTA
23. Sternal angle : T4-T5. Pectinate muscle present in Rt atrium
24. Intercostobrachial artery arises from posterolateral part of Descending aorta
25. RCA is involved in complete heart block. Pulmonary varix opens into LA
26. During needle thoracotomy nerve is injured 1st
27. For CVP reference point is : Manubriosternal Junction / 2nd costal cartilage or 4th ICS
28. Subcostal nerve carries pain from inferior lower segment of diaphragm
29. Both sides of 5th ICS supplied by Thoracic aorta
30. Thyroglossal cyst location: INFRA HYOID > THYROID REGION
31. Thoracic vertebrae are heart shaped
32. Thyroid gland runs from : C5 – T1
33. Median arcuate ligament formed by Diaphragm
34. Phrenic nerve passes Infront of Pulmonary artery
35. Internal thoracic artery supplies first 6 intercostal spaces anteriorly
36. Lower intercostal spaces supplied by : musculophrenic artery
37. Inferior thyroid artery supplies Thymus
38. Posterior surface/base of HEART supplied by 2 arteries
39. Bucket handle inc Transverse diameter of ribs cage while Pump handle inc AP diameter
40. Isthmus of thyroid situated over : 2nd-4th tracheal rings
41. Thymus extends from inferior border of Thyroid till C4
42. Brachiocephalic vein is formed by IJV + Subclavian vein behind sternal end of clavicle
43. Thyroid drains into DEEP cervical nodes
44. In coronary circulation, arteries run in respective AV grooves
45. Great cardiac vein drains into coronary sinus and becomes a part of it
46. Fibres of External ICM interdigitate with Serratus Anterior.
47. Bronchial cyst presents in Middle mediastinum
48. Forced expiration : Internal ICM > Rectus abdominus
49. Bronchial arteries supply pleura, Connective tissue/ Parenchyma of lungs. Pulmonary arteries supply Alveoli.
50. Mesothelium covering the lungs form : Visceral layer of Pleura
51. Branches of intercostal nerves are peritoneal (Sensory)
52. Esophagus has Striated epithelium throughout whole length
53. Esophagus has mixed muscles smooth + striated in middle

54. Venous drainage of Heart mainly by CORONARY SINUS (2/3 rd of heart)
55. Nerve lying lateral to trachea is VAGUS . Nerve having immediate relation with trachea : RLN
56. In profuse bleeding from Transverse cervical artery : Ligate thyrocervical trunk.
57. Pressure at 10 cm H ₂ O by PEEP will cause : Pneumothorax
58. Esophagus in thoracic area is constricted due to Arch of aorta
59. Arch of aorta lies anterior to Trachea
60. Quadratus lumborum attaches posteriorly to lateral arcuate ligaments
61. C4 gives largest share to Phrenic nerve
62. Collateral branches of intercostal nerves give lateral cutaneous branches
63. Stab wound at right of Linea alba will damage IVC
64. Arrangement in ICS from above downwards : VAN → vein, artery, and nerve
65. Left/ right dominant supply of heart is determined by – Posterior interventricular (Descending)
66. Great Cardiac vein accompany -Left ant. Descending Artery
67. Middle Cardiac vein accompany Post. Interventricular artery
68. Small Cardiac vein accompany- Marginal artery
69. Ant. Cardiac vein drains directly into – Right Atrium
70. Left lobe-5cm and Right Lobe 2.5cm
71. Pain of angina from heart is carried by – Sympathetic nerves. Pain of pericarditis is carried by – Phrenic nerve
72. Fibrous Pericardium and Parietal layer of Serous Pericardium is supplied by Phrenic nerve
73. Costal pleura – Intercostal Nerve. Mediastinal pleura purely by phrenic nerve.
74. Diaphragmatic pleura : Dome partly by Phrenic nerve and peripheral part by Lower Six intercostal.
75. Phrenic nerve damage Ipsilateral Diaphragm paralysis > Loss of central tendon sensation
76. Visceral layer of serous pericardium is called Epicardium. Pericardium is present b/w fibrous & Visceral layer.
77. Absence of cartilage in respiratory and terminal ducts differentiated it from TRACHEA
78. Lesser occipital & Greater auricular are cutaneous branches of CERVICAL PLEXUS
79. Thymus contains no Lymph nodes and Thymus works by PARACRINE action
80. Ext oblique arises from RIBS 5 – 12. Notching on CXR seen due to POST DUCTAL coarctation of aorta
81. Azygos vein opens into SVC at angle of Louis
82. Right Middle lobe has only 2 segments
83. Quite breathing + inc AP diameter by External ICM
84. Emboli in venous circulation will lodge in Pulmonary artery/ Lung. Emboli will 1 st go to IVC > RT ATRIUM
85. Cervical rib arises from C7 And CompressT1
86. Epicardium supplied by – Coronary Artery and Pericardium supplied by Pericardiophrenic artery
87. Anterior 2/3 rd IV Septum supplied by -LAD (LCA) and Posterior 1/3 rd IV Septum supplied by -PDA (RCA)
88. Left Circumflex supply – Left atrium and left Ventricle
89. Xiphisternum Vertebrae level-T9, (T7 is dermatome level)
90. IVC begin at-L5, extent from T8-L5
91. TrueRibs-1-7 ; FalseRibs-8-10 ; Floating Ribs -11-12
92. Upper Esophagus supplied by – Inferior Thyroid artery. Middle Esophagus – Descending thoracic aorta
93. Lower Esophagus-Left Gastric
94. Azygos Vein anterior to Right root of lung. Des Aorta posterior to root of left lung
95. Phrenic nerve anterior to Root of both lungs and Vagus Nerve posterior to Root of both Lung
96. IVC Blocked Above Azygous vein dilation in – Azygous vein > Left Gastric Vein
97. IVC Blocked Up to Azygous vein dilation in – Right. Ascending Lumbar vein & Right Subcostal
98. IVC Blocked Below Azygous vein dilation in – Ascending Lumbar vein
99. T8 – Caval Opening – Inferior Vena Cava and Right Phrenic Nerve
100.T10: Umbilicus , Esophageal Hiatus (Esophagus, Esophageal vessels, and Vagus nerves
101.T12 – Aortic Opening (Aorta, Azygous, and Thoracic Duct)
102.T3 toT6: Oblique Fissure of Lung. T4-5- Bifurcation of Trachea, Dermatome Nipple. Extent of Trachea C6-T4
103.C3 Hyoid in erect position
104.C2-C3 (C2 > C3)Tracheal ring Tracheostomy Level Adults. C3-C4 (C3>C4)Tracheal ring – Tracheostomy Level Children
105.Arch of Aorta is Anterior to left lung root . Descending aorta is posterior to left lung root
106.Tumor at Lt lung hilum compresses posteriorly Descending aorta > Vagus nerve > aorta
107.Infection of pre-tracheal fascia travels to anterior mediastinum

108. Infection related to Prevertebral fascia may spread to Superior Mediastinum
109. Subcostal/ subxiphoid approach is best for Pericardiocentesis, other is 5 th ICS lateral to sternum
110. For pleural tap: 9 th ICS lower border but Upper border of lower rib in midaxillary line
111. Needle thoracocentesis: At 2 nd ICS in MCL
112. Triangle of SAFETY: From 4 th – 6 th ICS; 5 th ICS is the best option.
113. At 6 th costal cartilage: RT ATRIUM while at 6 th ICS -- IVC
114. Injury at 4 th ICS: damage to intercostal membrane and Injury at 5 th ICS: damage to Intercostal muscles
115. Apex of Lung is 2.5cm above MCL
116. Rt bronchial artery given by 3 rd posterior ICA
117. Lt bronchial artery by descending aorta
118. Eparterial bronchus supplies: RT SUPERIOR LOBE and Hyparterial bronchus is inferior to Pulmonary artery.
119. C6- Cricoid Level (Esophagus and Trachea Starts). C2-3- Supraclavicular and C3-4 – Infraclavicular
120. Esophagus Passed through – Left Crus of Diaphragm
121. Medial Arcuate ligament formed by – Psoas Muscle fascia. Median Arcuate ligament formed by – Right & Left Crura
122. Moderator band is present in Right ventricle
123. Neurovascular bundle located at lower border of upper rib
124. Thoracic duct empties into: Venous system near union of left internal jugular vein and left subclavian vein, left venous angle and Origin of left brachiocephalic vein
125. Lower respiratory component sympathetic supply via T2- T4
126. Aorta gives bronchial artery at T5- T6
127. Artery of Adamkiewicz arises at = T9 - T12
128. Inferior wall MI: Right marginal branch of RCA involved
129. Lateral wall MI: LCX branch of LCA involved. Anterior wall MI: LAD branch of LCA involved
130. Posterior wall PDA branch of RCA involved
131. SA NODE AND AV NODE: supplied by RCA
132. Newborn thorax shape: ROUND
133. Contraction of diaphragm causes inc in intrathoracic Volume
134. Pulmonary Vein lies anterior to Pulmonary artery.
135. Oesophagostomy done and part of stomach mobilized up in thorax: now, it will be supplied by right gastroepiploic artery > Rt Gastric artery
136. Superior wall of thoracic cavity is formed by Suprapleural membrane
137. Cervical rib arises from ANTERIOR tubercle of transverse process of 7 th cervical vertebra
138. After rib incision the rib regenerates from osteogenic layer of periosteum
139. Thoracic outlet syndrome: most of the symptoms are caused by pressure on the LOWER trunk of brachial plexus
140. Anterior intercostal membrane replaces the external intercostal at the level of costal cartilage
141. Posterior intercostal membrane replaces the internal intercostal at the level of angle of ribs
142. The 10 th and 11 th intercostal nerves pass directly into the abdominal wall coz the ribs are floating
143. First intercostal nerve has no anterior cutaneous branch
144. For the intercostal nerve block the needle is inserted near the lower border of the rib instead of upper border
145. Suprapleural membrane is thickening of Endothoracic fascia. It is triangular and attached to medial border of 1 st rib laterally(base) and tip of transverse process of C7 medially(apex).
146. Some of muscle fibres of Right crus of diaphragm pass up to the left and surround Esophageal orifice like a sling.
147. Most commonly fractured ribs are 5 to 10.
148. Rib 1 to 4 are protected by clavicle, pecs, and scapula. 11 and 12 move along the force.
149. Diaphragm is also a weightlifting muscle
150. In most posterior part of intercostal space, the neurovascular bundle lies in the middle of the space. it comes along the lower border of rib above at the level of angle of the rib
151. Accessory phrenic nerve is branch from nerve to Subclavius (C5)
152. Clavicle is subcutaneous through its whole length
153. Apex beat is produced by straightening of aorta by the force of blood during vent contraction. This causes pushing of heart forwards producing apex beat.
154. First spine of vertebrae is of C7
155. Cardiac notch is present in upper lobe of Left lung
156. Costochondral joint = Cartilaginous + Amphiarthrosis

157. Hydrostatic pressure is greater in capillaries of parietal pleura than in visceral pleura. So pleural fluid is absorbed in visceral pleura
158. Presence of 300 ml of fluid in Costodiaphragmatic recess is sufficient to be detected clinically
159. During expiration the bifurcation of trachea moves up by one vertebral level. during deep inspiration it moves down as far as T6
160. Sensory nerve supply of trachea is from Vagi and recurrent laryngeal nerves. Sympathetic supply the trachealis
161. Mucosa of trachea is supplied by recurrent laryngeal nerve and in the region of bifurcation by pulmonary plexus
162. Bronchoscope can reach upto 1 st segmental bronchus
163. Females rely mainly on the movement of ribs rather than descent of diaphragm during inspiration.
164. Pericarditis is inflammation of serous pericardium
165. Floor of fossa Ovalis represents persistent septum primum. Annulus of fossa Ovalis represents septum secundum
166. Cusps of heart valves are formed by folds of endocardium with some connective tissue in core
167. SA node lies right to the SVC
168. Right border of heart is formed by RA. Right border of mediastinum in the X-ray is formed by right brachiocephalic vein, SVC, RA, and sometimes the IVC.
169. Size of Heart is = fist size (300gm)
170. Pulmonary Vein, SVC, Sinuses of brain and IJV are valve less
171. Location of SA node : Upper end of CRISTA TERMINALIS > Upper end of Sulcus Terminalis or Sub-Epicardium
172. AV node located at : endocardium. Conduction system of Heart : Sub endocardium
173. Costochondral joints : primary cartilaginous joints. Sternocostal joints : (synovial plane, Except 1 st)
174. Manubriosternal joint : (2ndry cartilaginous/ contains fibrocartilage)
175. Middle mediastinum contains bifurcation of Trachea
176. Posterior 1/3 rd IVS supply by : RCA
177. Pt with Hydrothorax due to pleurisy, sits up in bed the fluid will accumulate in : Costodiaphragmatic recess
178. Downward traction of AV valves can't be made in ; Chordae tendineae rupture
179. While ligating Int thoracic artery structure to be saved is Ipsilateral phrenic nerve
180. Descending thoracic aorta begins at lower border of T4
181. MCC of bleed during tracheostomy is Inferior thyroid vein ; in Heavy bleed: ant jugular vein
182. In child risk of damage to Left Brachiocephalic vein & Rt brachiocephalic trunk
183. Pt after RTA needs no Mech ventilation, if injury is -- below C5
184. Angle of Rib is most prone to be fractured.
185. Imperforate anus is due to failure of descent of the Urorectal septum, can be associated with other anomalies such as Esophageal Atresia and cardiac anomalies.

ABDOMEN, PELVIS & PERINEUM

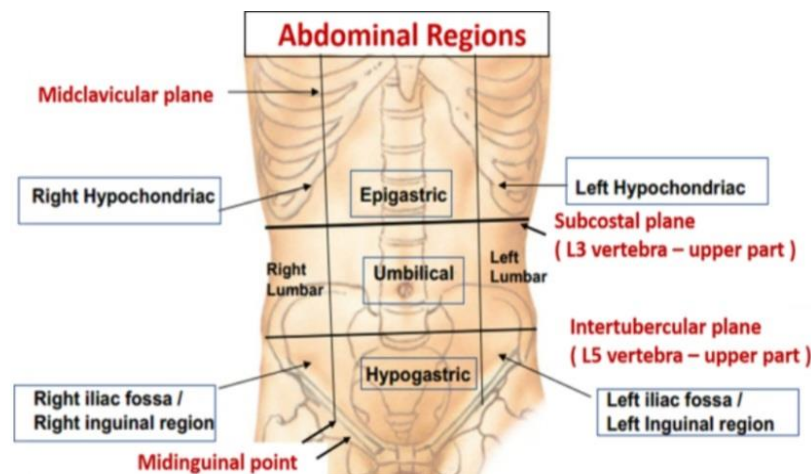
LAYERS OF ANTERIOR ABDOMINAL WALL

- Skin
- Superficial Fascia → having 2 layers :
Superficial Fatty layer (Camper Fascia) and Deep membranous layer (**Scarpa Fascia**)
- External Oblique muscle, Internal Oblique muscle, Transverse Abdominus muscle
- Fascia Transversalis or Endoabdominal fascia
- Extraperitoneal Fat and Parietal peritoneum
- **No Layer of Deep Fascia Exists** (to allow bulging during coughing, straining, and, pregnancy)
- Attachment of Scarpa's fascia:
- From the lower half of anterior abdominal wall, it passes over the inguinal ligament and is attached to the deep fascia of the thigh along a Horizontal line (Holden's line Approx. 8cm.) passing laterally from the pubic tubercle.
- **Medially** it passes downwards over the body of the pubis and becomes continuous with the superficial perineal fascia (Colle's fascia).
- The superficial perineal fascia is attached laterally to conjoint Ischiopubic rami and posteriorly it is fused with the Posterior border of perineal Membrane.
- It also **extends into the penis and Scrotum** (labia majora in females).
- Number of layers crossed when a cannula is inserted in different body regions:
- Abdomen (midline) **7 layers**, while Abdomen (in flank region) 9 layers
- Scrotum 7 layers, spinal tap 8 layers
- **Thorax: 8 layers** (if Endothoracic fascia and partial pleura are taken as a single layer then 7 layers)

QUADRANTS / REGIONS OF ABDOMEN (9)

Two Horizontal & 2 Vertical planes divide abdomen into 9 Quadrants as given below.

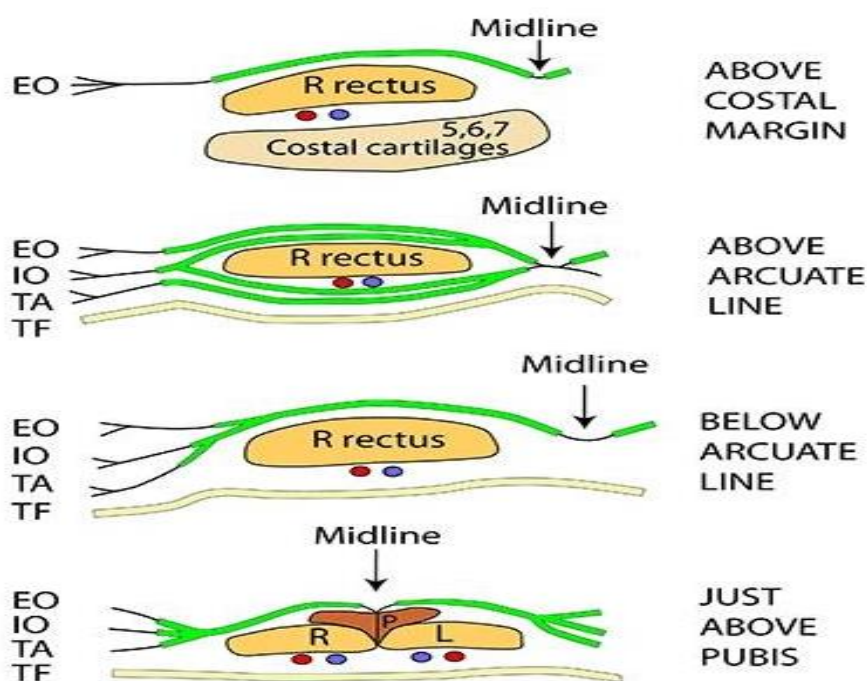
Two horizontal planes	<ul style="list-style-type: none"> ○ <u>Transpyloric plane:</u> passes Infront through tips of 9th costal cartilages. Behind at lower border of L1 ○ <u>Subcostal plane:</u> passes Infront at level of inferior margin of 10th rib. Behind through upper L3
Two vertical planes	<ul style="list-style-type: none"> ○ Right and left midclavicular Planes pass through the mid- Point of clavicle to the midinguinal point (midway between anterior superior iliac spine and pubic symphysis). ○ Femoral artery pulsations can be felt at Mid inguinal point.



Important plane	Vertebral level
Transpyloric plane	<ul style="list-style-type: none"> ○ At Lower border of L1 (horizontal line halfway b/w Suprasternal notch and Pubic symphysis) ○ Structures passing at the level of Transpyloric plane are: Pylorus of stomach, Neck of pancreas, Duodeno- Jejunal flexure, Fundus of gall bladder, Hilum of kidneys, Origin of superior mesenteric artery, Tip of ninth costal cartilage, Termination of spinal cord, sphincter of Oddi
Subcostal plane	○ Upper part of Body of L3 vertebra
Supracristal plane	○ Plane passing through the highest point of iliac crest: L4 Vertebra
Intertubercular plane	○ Upper Part of body of L5 vertebra
Bloody supply of Anterior abdominal wall	<ol style="list-style-type: none"> 1. Superior epigastric, branch of internal thoracic artery 2. Lateral cutaneous branches of posterior intercostal arteries 3. Superficial epigastric branch of femoral artery 4. Inferior epigastric branch of external iliac artery. 5. Deep circumflex branch of external iliac artery
Nerve supply	<ul style="list-style-type: none"> • Anterior cutaneous branches of T7-T11 intercostal nerves and subcostal nerve. • Lateral cutaneous branches of T10 and T11 intercostal nerves • iliohypogastric nerve
Lymphatic drainage	Lymphatics from anterior abdominal wall: <ul style="list-style-type: none"> ■ above the level of umbilicus drains into axillary lymph nodes. ■ below the level of umbilicus drains into superficial inguinal lymph nodes.

Abdominal wall muscles				
Muscle	Origin	Insertion	Innervation	Action
Anterior abdominal wall muscles				
① Rectus abdominis	Pubis (between pubic tubercle and symphysis)	Cartilages of 5th to 7th ribs, xiphoid process of sternum	Intercostal nn. (T5–T12)	Flexes trunk, compresses abdomen, stabilizes pelvis
② Pyramidalis	Pubis (anterior to rectus abdominis)	Linea alba (runs within the rectus sheath)	Subcostal n. (12th intercostal n.)	Tenses linea alba
Anterolateral abdominal wall muscles				
③ External oblique	5th to 12th ribs (outer surface)	Linea alba, pubic tubercle, anterior iliac crest	Intercostal nn. (T7–T12)	<i>Unilateral:</i> Bends trunk to same side, rotates trunk to opposite side
④ Internal oblique	Thoracolumbar fascia (deep layer), iliac crest (intermediate line), anterior superior iliac spine, iliopsoas fascia	10th to 12th ribs (lower borders), linea alba (anterior and posterior layers)	Intercostal nn. (T7–T12), iliohypogastric n., ilioinguinal n.	<i>Bilateral:</i> Flexes trunk, compresses abdomen, stabilizes pelvis
⑤ Transversus abdominis	7th to 12th costal cartilages (inner surfaces), thoracolumbar fascia (deep layer), iliac crest, anterior superior iliac spine (inner lip), iliopsoas fascia	Linea alba, pubic crest		<i>Unilateral:</i> Rotates trunk to same side <i>Bilateral:</i> Compresses abdomen
Posterior abdominal wall muscles				
⑥ Psoas major	Superficial layer	T12–L4 vertebral bodies and associated intervertebral disks (lateral surfaces)	Direct branches from lumbar plexus (L2–L4)	Hip joint: Flexion and external rotation Lumbar spine (with femur fixed): <i>Unilateral:</i> Contraction bends trunk laterally
	Deep layer	L1–L5 (costal processes)		<i>Bilateral:</i> Contraction raises trunk from supine position
⑦ Iliacus	Iliac fossa		Femoral n. (L2–L4)	
⑧ Quadratus lumborum	Iliac crest and iliolumbar ligament (not shown)	12th rib, L1–L4 vertebrae (transverse processes)	T12, L1–L4 spinal nn.	<i>Unilateral:</i> Bends trunk to same side <i>Bilateral:</i> Bearing down and expiration, stabilizes 12th rib

RECTUS SHEATH	
	<ul style="list-style-type: none"> 3-5cm below Umbilicus is the Arcuate Line (Semi-circular Line) Lateral edge of rectus sheath is called Linea Semilunaris
Above Arcuate Line:	<ul style="list-style-type: none"> Anterior Layer formed by: (EO + IO) External Oblique Aponeurosis + Anterior Lamina of Internal Oblique's Aponeurosis Posterior Layer formed by: (IO + TA) Posterior Lamina of Internal Oblique Aponeurosis + Transversus Abdominis Aponeurosis
Below Arcuate Line:	<ul style="list-style-type: none"> Anterior Layer formed by: (EO + IO + TA) External Oblique Aponeurosis + Internal Oblique aponeurosis + Transversus Abdominis Aponeurosis. Posterior Layer: Only Transversalis Fascia (TF)
Contents	<ul style="list-style-type: none"> Muscles: Rectus Abdominis + Pyramidalis, Vessels: Superior and Inferior Epigastric vessels Nerves: Lower 5 Intercostal Nerves and Subcostal Nerve



Key Facts

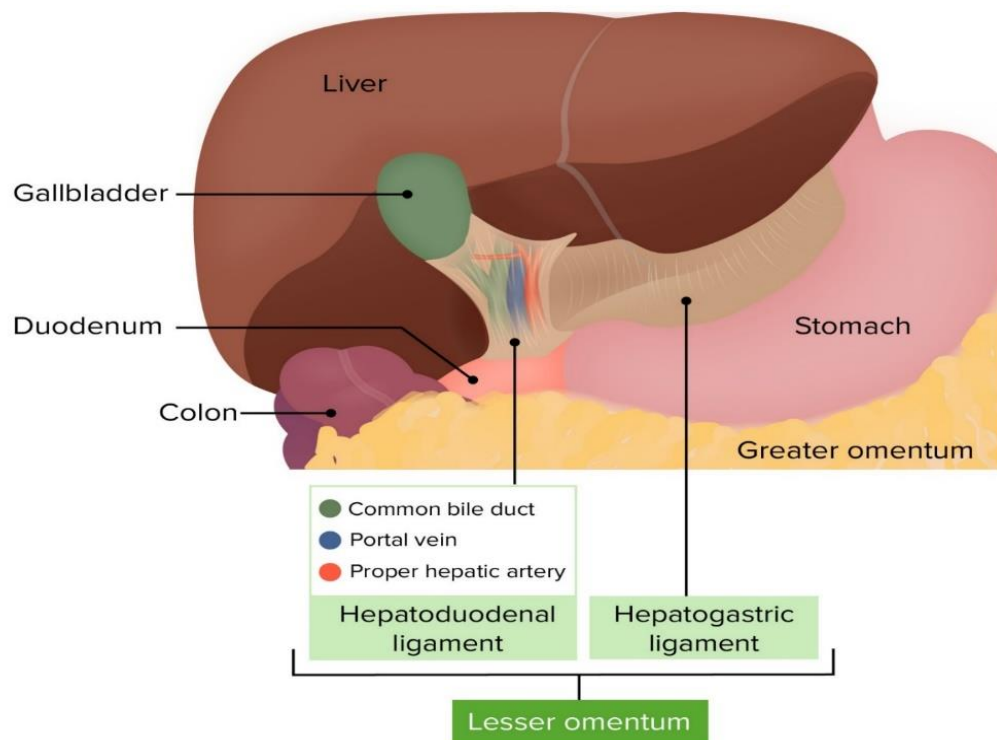
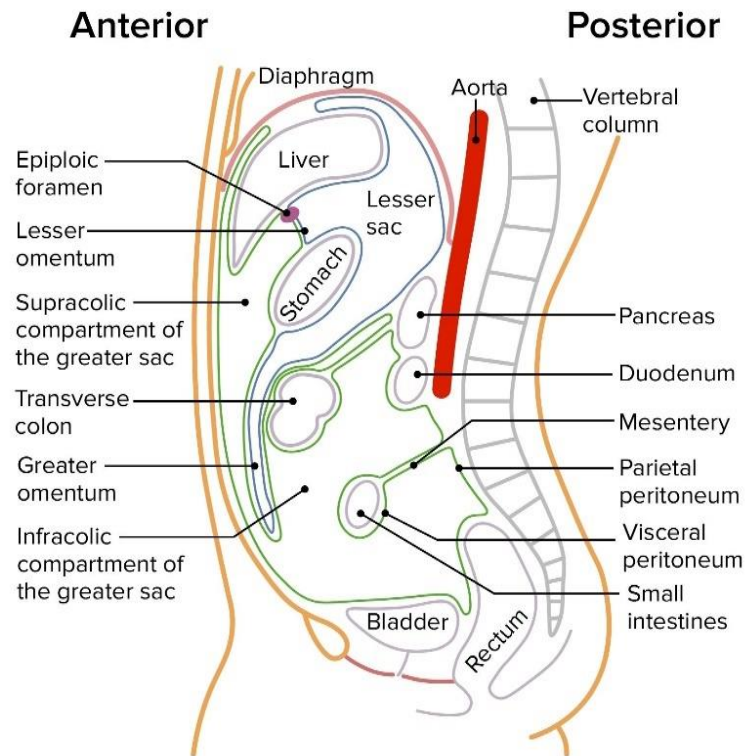
✚	Superficial inguinal ring is made of EO muscle fibres
✚	Deep inguinal ring is formed by Transversalis fascia
✚	Inguinal ligament extends from ASIS to Pubic Tubercle
✚	External spermatic fascia (arising from the external oblique aponeurosis)
✚	cremaster fascia which contains the cremaster muscle (arises from the internal oblique muscle aponeurosis)
✚	internal spermatic fascia (arising from the transversalis fascia)
✚	Dartos fascia contains smooth muscles.
✚	Pyramidalis muscle is supplied by T12 (subcostal nerve)
✚	Arcuate line is the inferior extent of rectus sheath

PERITONEUM	
Layers of peritoneum	<ul style="list-style-type: none"> ○ A Serous membrane lining viscera and abdominal cavity and has 2 layers or Parts. ○ Parietal Peritoneum: outer serous membrane containing Somatic and Intercostal nerves. ○ Visceral Peritoneum: inner serous membrane covering organs and sensitive to Stretch. ○ It forms all mesenteries. Space b/w parietal and Visceral layer is called Peritoneal cavity. ○ Peritoneum is lined by Mesothelium (a Derivative of Mesoderm)
Peritoneal Formations	<ol style="list-style-type: none"> 1. Mesentery: mesentery proper, transverse mesocolon, sigmoid mesocolon, and , mesoappendix 2. Omenta: greater omentum, lesser omentum 3. Peritoneal ligaments: hepatogastric, hepatoduodenal, gastrophrenic, gastrosplenic, splenorenal and gastrocolic ligament
Divisions	<ul style="list-style-type: none"> ○ Lesser sac (omental bursa) and Greater sac (supracolic and infracolic compartments)
Functions	<ul style="list-style-type: none"> ○ Protection of the abdominopelvic organs and connect organs with each other. ○ Maintains the position of organs by suspending them with ligaments and prevents friction

FORMATIONS OF PERITONEUM							
MESENTERY	<ul style="list-style-type: none"> ○ Folds of peritoneum connecting viscera or intestines to abdominal wall ○ Small bowel mesentery is 6 inches long (15cm) runs from Left L2 transverse process to Rt Sacroiliac joint , crossing Aorta , IVC , Psoas muscles , Right Ureter & Rt common iliac bifurcation <table> <tr> <td>Intraperitoneal organs</td><td> <ul style="list-style-type: none"> ❖ Completely covered with visceral peritoneum Examples are: ❖ Stomach, Spleen, liver, gallbladder, duodenum 1st part, jejunum, ileum, appendix, transverse and sigmoid colon, tail of pancreas </td></tr> <tr> <td>Retroperitoneal organs</td><td> <ul style="list-style-type: none"> ❖ Found between the parietal Peritoneum and the posterior abdominal wall. ❖ Covered by peritoneum only on its anterior surface (e.g., kidney) ❖ Major primary retroperitoneal organs never had a mesentery, Examples are Kidneys, adrenal glands, ureters, aorta, IVC, lower rectum, anal canal. ❖ Major Secondary retroperitoneal organs -lost mesentery during development ❖ Examples: duodenum (2nd , 3rd part), Pancreas (head, neck, and body), ascending and descending colon, upper rectum ❖ Mnemonics For Retroperitoneal Organs= SAD PUCKER ❖ Suprarenal gland, Aorta, IVC, Duodenum, Pancreas, Ureter, Colon, Kidney, Esophagus and Rectum </td></tr> <tr> <td>Subperitoneal organs</td><td> <p>Covered by peritoneum only on its superior surface</p> <p>Example: Urinary bladder</p> </td></tr> </table>	Intraperitoneal organs	<ul style="list-style-type: none"> ❖ Completely covered with visceral peritoneum Examples are: ❖ Stomach, Spleen, liver, gallbladder, duodenum 1st part, jejunum, ileum, appendix, transverse and sigmoid colon, tail of pancreas 	Retroperitoneal organs	<ul style="list-style-type: none"> ❖ Found between the parietal Peritoneum and the posterior abdominal wall. ❖ Covered by peritoneum only on its anterior surface (e.g., kidney) ❖ Major primary retroperitoneal organs never had a mesentery, Examples are Kidneys, adrenal glands, ureters, aorta, IVC, lower rectum, anal canal. ❖ Major Secondary retroperitoneal organs -lost mesentery during development ❖ Examples: duodenum (2nd , 3rd part), Pancreas (head, neck, and body), ascending and descending colon, upper rectum ❖ Mnemonics For Retroperitoneal Organs= SAD PUCKER ❖ Suprarenal gland, Aorta, IVC, Duodenum, Pancreas, Ureter, Colon, Kidney, Esophagus and Rectum 	Subperitoneal organs	<p>Covered by peritoneum only on its superior surface</p> <p>Example: Urinary bladder</p>
Intraperitoneal organs	<ul style="list-style-type: none"> ❖ Completely covered with visceral peritoneum Examples are: ❖ Stomach, Spleen, liver, gallbladder, duodenum 1st part, jejunum, ileum, appendix, transverse and sigmoid colon, tail of pancreas 						
Retroperitoneal organs	<ul style="list-style-type: none"> ❖ Found between the parietal Peritoneum and the posterior abdominal wall. ❖ Covered by peritoneum only on its anterior surface (e.g., kidney) ❖ Major primary retroperitoneal organs never had a mesentery, Examples are Kidneys, adrenal glands, ureters, aorta, IVC, lower rectum, anal canal. ❖ Major Secondary retroperitoneal organs -lost mesentery during development ❖ Examples: duodenum (2nd , 3rd part), Pancreas (head, neck, and body), ascending and descending colon, upper rectum ❖ Mnemonics For Retroperitoneal Organs= SAD PUCKER ❖ Suprarenal gland, Aorta, IVC, Duodenum, Pancreas, Ureter, Colon, Kidney, Esophagus and Rectum 						
Subperitoneal organs	<p>Covered by peritoneum only on its superior surface</p> <p>Example: Urinary bladder</p>						
OMENTA	<table> <tr> <td>Greater Omentum</td><td> <ul style="list-style-type: none"> ○ A large fold of peritoneum which hangs down from the Greater curvature of the stomach like an apron and covers the loops of intestines to a varying extent. ○ Made up of 4 layers. ○ Contents are Right and left gastroepiploic vessels + Fat. ○ Functions : storehouse of fat, protects the peritoneal cavity against infection (collection of macrophages form milky spots). ○ it is aka policeman of the abdomen </td></tr> <tr> <td>Lesser Omentum</td><td> <ul style="list-style-type: none"> ○ A fold of peritoneum extending from the lesser curvature of the stomach and the First 2 cm of the duodenum to the liver. ○ Attachments ○ Inferiorly: lesser curvature of stomach and duodenum ○ Superiorly: liver in the form of an inverted L' ○ Hepatogastric ligament: The portion of the lesser omentum between the less curvature of Stomach and the liver. ○ It contains the right and the left gastric arteries. </td></tr> </table>	Greater Omentum	<ul style="list-style-type: none"> ○ A large fold of peritoneum which hangs down from the Greater curvature of the stomach like an apron and covers the loops of intestines to a varying extent. ○ Made up of 4 layers. ○ Contents are Right and left gastroepiploic vessels + Fat. ○ Functions : storehouse of fat, protects the peritoneal cavity against infection (collection of macrophages form milky spots). ○ it is aka policeman of the abdomen 	Lesser Omentum	<ul style="list-style-type: none"> ○ A fold of peritoneum extending from the lesser curvature of the stomach and the First 2 cm of the duodenum to the liver. ○ Attachments ○ Inferiorly: lesser curvature of stomach and duodenum ○ Superiorly: liver in the form of an inverted L' ○ Hepatogastric ligament: The portion of the lesser omentum between the less curvature of Stomach and the liver. ○ It contains the right and the left gastric arteries. 		
Greater Omentum	<ul style="list-style-type: none"> ○ A large fold of peritoneum which hangs down from the Greater curvature of the stomach like an apron and covers the loops of intestines to a varying extent. ○ Made up of 4 layers. ○ Contents are Right and left gastroepiploic vessels + Fat. ○ Functions : storehouse of fat, protects the peritoneal cavity against infection (collection of macrophages form milky spots). ○ it is aka policeman of the abdomen 						
Lesser Omentum	<ul style="list-style-type: none"> ○ A fold of peritoneum extending from the lesser curvature of the stomach and the First 2 cm of the duodenum to the liver. ○ Attachments ○ Inferiorly: lesser curvature of stomach and duodenum ○ Superiorly: liver in the form of an inverted L' ○ Hepatogastric ligament: The portion of the lesser omentum between the less curvature of Stomach and the liver. ○ It contains the right and the left gastric arteries. 						

		<ul style="list-style-type: none"> ○ Hepatoduodenal ligament: the portion between the superior Duodenum and porta hepatis of the liver. Manual compression of the hepatoduodenal ligament during surgery is known as The Pringle's Manoeuvre ○ Contents: <ul style="list-style-type: none"> ❖ The right free margin of the lesser omentum or Hepatoduodenal ligament contains: <ul style="list-style-type: none"> ✓ The proper hepatic artery medially and anteriorly ✓ The portal vein posteriorly ✓ The bile duct Laterally ✓ Lymph nodes & lymphatics with Hepatic plexus of nerves
LIGAMENTS	Dorsal Mesogastrium	<p>Extends from the greater curvature to the posterior abdominal wall.</p> <p>Derivatives:</p> <ul style="list-style-type: none"> ▪ Spleen ▪ Gastrosplenic ligament contains the short gastric & left Gastro-epiploic vessels. ▪ Lienorenal ligament: contains the tail of pancreas & Splenic vessels) ▪ Greater omentum ▪ Cranial most part forms the gastrophrenic ligament
	Ventral Mesogastrium	<ul style="list-style-type: none"> ▪ Extends from the lesser curvature to septum transversum and anterior abdominal wall. Derivatives are as follows: <ul style="list-style-type: none"> ▪ Falciform ligament, Right and left triangular ligaments, Superior and inferior layers of coronary ligaments and Lesser omentum
DIVISIONS OF PERITONEUM		
Greater Sac	<ul style="list-style-type: none"> ○ Also known as the general cavity (of the abdomen) or peritoneum of the peritoneal cavity proper, is the cavity in the abdomen that is inside the peritoneum but outside the lesser sac. ○ Extends from the diaphragm to the pelvic cavity. ○ It is divided into the supracolic and infracolic compartments by the transverse mesocolon. ○ The supracolic compartment is found anterior and superior to the transverse mesocolon and contains the liver, stomach, and spleen. 	
Lesser Sac	<ul style="list-style-type: none"> ○ Also known as Omental bursa, Present Behind the stomach and lesser Omentum. Boundaries are: ○ Anterior wall: from above downward, By the caudate lobe of the liver, Lesser omentum, back of the stomach and the anterior two layers of the Greater omentum. ○ Posterior wall: from below upward by posterior two layers of the greater Omentum, transverse colon, transverse Mesocolon, upper surface of Pancreas, left adrenal gland and upper end of left kidney ○ Superiorly diaphragm and inferiorly extend till layers of Greater omentum fuse together. ○ Left margin of the sac is formed by Greater omentum, Spleen and Splenorenal ligament. ○ Right margin opens into the greater sac through opening of lesser sac (epiploic foramen). 	

Epiploic Foramen (Winslow's foramen)	<ul style="list-style-type: none"> ○ The passage between lesser and greater sac. ○ Greater + Lesser sac communicate by it. ○ Boundaries <ul style="list-style-type: none"> ❖ Anteriorly: Free border of lesser omentum ❖ Posteriorly: Inferior vena cava , T12 vertebrae ❖ Superiorly : Caudate process of the caudate lobe of liver ❖ Inferiorly : First part of the Duodenum
Hepatorenal pouch (Morrison's pouch)	<ul style="list-style-type: none"> ○ Most dependent (gravitationally) part of peritoneal cavity in supine position. ○ It is the Right Posterior Subhepatic space. ○ Boundaries <ul style="list-style-type: none"> ❖ Anterior: Right lobe of liver, gallbladder ❖ Posteriorly: 2nd part of duodenum, right flexure of colon, head of pancreas ❖ Superior: Inferior layer of coronary ligament ❖ Inferiorly: Opens to the general peritoneal cavity ✓ Fluid accumulation in Abdominal cavity occurs in this pouch mostly.



KEY FACTS

- Mass at Porta Hepatis will compress Portal Vein
- Hepatoma will early compress Portal Vein
- During surgery, nick at right of Hepatoduodenal ligament will cause injury to Bile Duct or CBD
- Carcinoma of Head of Pancreas will compress CBD
- A structure seen on endoscopy or ERCP, looping around going towards target organ is Rt hepatic artery
- Structures seen in Rt free margin of Epiploic foramina → Bile duct , portal vein , hepatic artery
- Cystic artery is a branch of Rt hepatic artery and supplied proximal bile duct
- Cystic artery is in Calot's triangle
- Tortuous Right hepatic artery is called Caterpillar or Moynihan's hump
- In open cholecystectomy cystic duct is sutured with VICRYL suture
- Right Hepatic artery > Left hepatic is damaged during cholecystectomy
- In case of 1cm stone of gallbladder : Observation is the best approach
- In acute pancreatitis Fluid accumulates in Lesser sac
- In ruptured ectopic pregnancy, accumulation of fluid or blood occurs in Rectouterine or pouch of Douglas
- After Cholecystectomy drain should be placed in Right SUBHEPATIC space
- After Appendectomy, drain needs to be placed in SUB PHRRNIC space
- In Anterior duodenal perforation, drain to be placed in RIGHT ILIAC FOSSA > Rt PARACOLIC gutter
- In posterior duodenal perforation, drain to be placed in LESSER SAC
- In hydrocele , fluid accumulated in TUNICA VAGINALIS
- Post cholecystectomy , asthmatic patient , KETOROLAC (Inj Toradol) is preferred choice as painkiller
- In acute pancreatitis PETHIDINE is preferred (P for Pancreatitis & Pethidine)
- Less bile after cholecystectomy will lead to Steatorrhea
- In case of Bile Duct injury GGT is raised

Foregut	Midgut	Hindgut
Artery: celiac	Artery: superior mesenteric	Artery: inferior mesenteric
Parasympathetic innervation: vagus nerves	Parasympathetic innervation: vagus nerves	Parasympathetic innervation: pelvic splanchnic nerves
Sympathetic innervation: <ul style="list-style-type: none"> Preganglionics: thoracic splanchnic nerves, T5–T9 Postganglionic cell bodies: celiac ganglion 	Sympathetic innervation: <ul style="list-style-type: none"> Preganglionics: thoracic splanchnic nerves, T9–T12 Postganglionic cell bodies: superior mesenteric ganglion 	Sympathetic innervation: <ul style="list-style-type: none"> Preganglionics: lumbar splanchnic nerves, L1–L2 Postganglionic cell bodies: inferior mesenteric ganglion
Referred Pain: Epigastrium	Referred Pain: Umbilical	Referred Pain: Hypogastrium
Foregut Derivatives	Midgut Derivatives	Hindgut Derivatives
Esophagus	Duodenum (second, third, and fourth parts)	Transverse colon (distal third—splenic flexure)
Stomach	Jejunum	Descending colon
Duodenum (first and second parts)	Ileum	Sigmoid colon
Liver	Cecum	Rectum
Pancreas	Appendix	Anal canal (above pectinate line)
Biliary apparatus	Ascending colon	
Gallbladder	Transverse colon (proximal two-thirds)	

ESOPHAGUS								
General features	<ul style="list-style-type: none">10 inches (25 cm) muscular tube Beginning at the lower border of cricoid cartilage (C6)passes through diaphragm at T10 level to enter Stomach and It is collapsed at restThe esophagus has three anatomical and physiological constrictionThe average life of gastrointestinal epithelium is 2-7 daysDilation or enlargement of left atrium cause esophageal obstruction or dysphagiaEsophagus pass through left Crus of diaphragm with sling of fibres from right crusAt rest, the esophagus is closed at both ends by the upper esophageal sphincter at the top and the lower esophageal sphincter at the bottomGastroesophageal sphincter is Not an anatomic sphincter, exists at the lower end of the esophagus. However, the circular laver of smooth muscle in this region serves as a physiologic sphincter. Metoclopramide maintain competence of GEJ and given in Diabetic GastroparesisThe wall of consists of four layers: Mucosa, Submucosa, Muscularis propria, And Adventitia.Unlike other areas of the GI tract, the esophagus does not have a distinct Serosal coveringEpithelium – Stratified squamous non keratinized epitheliumThe Upper third of the muscularis externa of esophagus contains skeletal musclesThe middle third of the muscularis externa contains skeletal muscles and Smooth musclesThe lower third of the muscularis externa contain only smooth muscles							
Constrictions	<p>4 sites of anatomical constrictions , The Distance of each is measured from upper incisor teeth.</p> <table><tr><td>Cricopharyngeus</td><td>1stconstriction, narrowest, 15 cm (6 inches) from upper incisor at level of C6</td></tr><tr><td>Aortico-bronchus</td><td>It is Divided as: Aortic -2nd constriction, at crossing of arch of aorta, vertebral T4, 22 cm from the upper incisor teeth Bronchial : middle one, 3rd constriction, at crossing of left Principal bronchus, vertebral level-T6, 27 cm from the upper incisor</td></tr><tr><td>Diaphragmatic</td><td>4h constriction 40 cm (15 inches) from the upper incisor , at level of T10</td></tr></table>		Cricopharyngeus	1 st constriction, narrowest, 15 cm (6 inches) from upper incisor at level of C6	Aortico-bronchus	It is Divided as: Aortic -2nd constriction, at crossing of arch of aorta, vertebral T4, 22 cm from the upper incisor teeth Bronchial : middle one, 3rd constriction, at crossing of left Principal bronchus, vertebral level-T6, 27 cm from the upper incisor	Diaphragmatic	4h constriction 40 cm (15 inches) from the upper incisor , at level of T10
Cricopharyngeus	1 st constriction, narrowest, 15 cm (6 inches) from upper incisor at level of C6							
Aortico-bronchus	It is Divided as: Aortic -2nd constriction, at crossing of arch of aorta, vertebral T4, 22 cm from the upper incisor teeth Bronchial : middle one, 3rd constriction, at crossing of left Principal bronchus, vertebral level-T6, 27 cm from the upper incisor							
Diaphragmatic	4h constriction 40 cm (15 inches) from the upper incisor , at level of T10							
Neurovascular supply and lymphatics	<table><tr><td>Upper 1/3rd</td><td>Inferior thyroid artery, inferior thyroid vein and Deep cervical lymph node</td></tr><tr><td>Middle 1/3rd</td><td>Descending thoracic aorta, Azygos vein, Mediastinal lymph nodes</td></tr><tr><td>Lower 1/3rd</td><td>Left gastric artery, left gastric vein, nodes -- left gastric and celiac</td></tr></table>	Upper 1/3 rd	Inferior thyroid artery, inferior thyroid vein and Deep cervical lymph node	Middle 1/3 rd	Descending thoracic aorta, Azygos vein, Mediastinal lymph nodes	Lower 1/3 rd	Left gastric artery, left gastric vein, nodes -- left gastric and celiac	
Upper 1/3 rd	Inferior thyroid artery, inferior thyroid vein and Deep cervical lymph node							
Middle 1/3 rd	Descending thoracic aorta, Azygos vein, Mediastinal lymph nodes							
Lower 1/3 rd	Left gastric artery, left gastric vein, nodes -- left gastric and celiac							

DEGLUTITION (SWALLOWING) PROCESS

- Food is passed from mouth through the Pharynx and esophagus into the stomach because of reflex phenomena. The swallowing reflex is coordinated in medulla.
- Fibers in vagus and Glossopharyngeal nerves Carry information between the GIT and the medulla.
- Deglutition can be Divided into three parts or stages as given below:

Voluntary stage	Pressure of tongue upward and backward against the Palate forces the bolus into the pharynx
Pharyngeal stage (involuntary)	<ul style="list-style-type: none"> Bolus in posterior mouth stimulates swallowing receptor area around the opening of Pharynx. Afferent impulses are transmitted through 9th (Glossopharyngeal) and 10th (vagus) cranial nerves to swallowing centre in medulla and lower pons. Efferent Impulses pass to pharynx and upper esophagus to cause the following effects: <ol style="list-style-type: none"> Soft palate Is pulled upward to close the posterior nares. Palatopharyngeal folds are pulled medially to form a sagittal slit which allows Properly masticated food to pass and prevents large particles to pass through it. Vocal cords are approximated (adducted) and larynx is pulled upward and anteriorly by Neck muscle. Vocal cords adduction is imp than Larynx movement upward and forward. Since the true vocal folds adduct during the swallow, a finite period of apnea (swallowing apnea) must necessarily take place with each swallow Peristalsis begins in the pharynx, which propels the food from pharynx into the Esophagus.
Esophageal stage	<p>3rd part of deglutition (involuntary), As the Food moves through esophagus into the stomach, three factors Participate in it:</p> <ul style="list-style-type: none"> Primary peristalsis: It is continuation of the peristaltic waves that begin in the Pharynx. It propels most of the bolus into the stomach.

	<ul style="list-style-type: none"> • Secondary peristalsis: The remaining bolus in the esophagus causes distension of the Esophagus ,Vagal reflex occurs which initiates secondary peristalsis in esophagus, and causes receptive relaxation of LES and remaining bolus is passed into the Stomach. The secondary peristaltic wave clears the esophagus of any remaining food. • Gravity (in standing position): Gravity increases the rate of passage of food through The esophagus but the movement of food in esophagus does not depend upon Gravity; food will still reach the stomach even if the person is upside down. ✓ Esophageal stage of swallowing is affected by Scleroderma
--	---

STOMACH

General Features	<ul style="list-style-type: none"> • Epithelium: Simple columnar epithelium without goblet cell • Develop as fusiform dilatation of caudal part of foregut in the middle of 4th week. • During the next 2 weeks, the right wall of the swelling grows more rapidly than the left Wall. • Stomach rotates at start of 5th week. • This leads to the formation of future greater omentum and lesser curvature of the adult. • The anterior border become lesser curvature and posterior/dorsal border becomes greater curvature 						
Parts	<ul style="list-style-type: none"> ○ Fundus is dome-shaped and projects upward and to left of the cardiac orifice. It is usually full of gas. ○ Body: This extends from the level of the cardiac orifice to the level of the incisura Angularis, a constant notch in the lower part of the lesser curvature. Mixing wave of stomach originate in body of stomach. ○ Pyloric antrum: This extends from the incisura angularis to the pylorus. ○ Pylorus: This is the most tubular part of the stomach. The thick muscular wall is called the Pyloric sphincter, and the cavity of the pylorus is the pyloric canal. ○ Circular muscle Becomes thickened at the level of pylorus and forms sphincter 						
Stomach Bed	<ul style="list-style-type: none"> ○ It contains tail of the pancreas, splenic artery, left kidney, left suprarenal gland, transverse colon and its mesocolon, and the left crus of diaphragm, and the left colic flexure. ○ Damage to Posterior wall erodes splenic artery that effects Fundus (Short gastric vessels arise from splenic) 						
Gastric glands	<table> <tr> <td>Parietal or oxyntic cells</td><td> <ul style="list-style-type: none"> • Found in the lining of the fundus > cardiac end of stomach. • Secrete HCL + intrinsic factor of castle (glycoprotein) • Contain copious Eosinophilic cytoplasm and central nucleus. • Parietal cells contain receptor for Gastrin, Histamine (H2) and acetylcholine (M3) • Somatostatin is the major paracrine hormone that inhibits gastric HCL secretion. • PPIs Irreversible bind to H⁺/K⁺ ATPase, cause blocking of all gastric acid Secretion • Antihistamine Block histamine receptors in Parietal cell, resulting in dec Acid </td></tr> <tr> <td>Chief or zymogen cells</td><td> <ul style="list-style-type: none"> • Abundant in fundus of stomach and Secrete Pepsinogen • Pepsinogen is converted into pepsin by HCL which causes digestion of protein. • Pepsin is stable in acidic solution below pH 6, but it is irreversibly denatured at pH 7 or above. In contrast, Pepsinogen is Stable in neutral or slightly alkaline solution </td></tr> <tr> <td>Mucoid cells</td><td> <ul style="list-style-type: none"> • Provide protective mucous coat that Protects against self-digestion by HCL </td></tr> </table>	Parietal or oxyntic cells	<ul style="list-style-type: none"> • Found in the lining of the fundus > cardiac end of stomach. • Secrete HCL + intrinsic factor of castle (glycoprotein) • Contain copious Eosinophilic cytoplasm and central nucleus. • Parietal cells contain receptor for Gastrin, Histamine (H2) and acetylcholine (M3) • Somatostatin is the major paracrine hormone that inhibits gastric HCL secretion. • PPIs Irreversible bind to H⁺/K⁺ ATPase, cause blocking of all gastric acid Secretion • Antihistamine Block histamine receptors in Parietal cell, resulting in dec Acid 	Chief or zymogen cells	<ul style="list-style-type: none"> • Abundant in fundus of stomach and Secrete Pepsinogen • Pepsinogen is converted into pepsin by HCL which causes digestion of protein. • Pepsin is stable in acidic solution below pH 6, but it is irreversibly denatured at pH 7 or above. In contrast, Pepsinogen is Stable in neutral or slightly alkaline solution 	Mucoid cells	<ul style="list-style-type: none"> • Provide protective mucous coat that Protects against self-digestion by HCL
Parietal or oxyntic cells	<ul style="list-style-type: none"> • Found in the lining of the fundus > cardiac end of stomach. • Secrete HCL + intrinsic factor of castle (glycoprotein) • Contain copious Eosinophilic cytoplasm and central nucleus. • Parietal cells contain receptor for Gastrin, Histamine (H2) and acetylcholine (M3) • Somatostatin is the major paracrine hormone that inhibits gastric HCL secretion. • PPIs Irreversible bind to H⁺/K⁺ ATPase, cause blocking of all gastric acid Secretion • Antihistamine Block histamine receptors in Parietal cell, resulting in dec Acid 						
Chief or zymogen cells	<ul style="list-style-type: none"> • Abundant in fundus of stomach and Secrete Pepsinogen • Pepsinogen is converted into pepsin by HCL which causes digestion of protein. • Pepsin is stable in acidic solution below pH 6, but it is irreversibly denatured at pH 7 or above. In contrast, Pepsinogen is Stable in neutral or slightly alkaline solution 						
Mucoid cells	<ul style="list-style-type: none"> • Provide protective mucous coat that Protects against self-digestion by HCL 						
Blood supply	<ul style="list-style-type: none"> ○ Short gastric vessels supply fundus. Left gastric supplies Lesser curvature, and Rt gastric supplies Pylorus. ○ Rt and Lt gastroepiploic supply greater curvature & Omentum ○ After Esophagectomy, the viability of the transposed stomach mainly depends on the right gastroepiploic artery and to lesser extent on the right gastric vessels 						
Venous drainage	<ul style="list-style-type: none"> ○ The veins drain into the portal circulation. ○ The left and right gastric veins drain directly into the portal vein. ○ The short gastric veins and the left gastroepiploic veins join the splenic vein. ○ The right gastroepiploic vein joins the superior mesenteric vein 						
Lymphatic drainage	<ul style="list-style-type: none"> ○ The lymph vessels follow the arteries into the left and right gastric nodes, the left and right Gastroepiploic nodes, and the short gastric nodes. ○ All lymph from the stomach eventually passes to the celiac nodes located around the root of the celiac artery on the posterior abdominal wall. ○ Celiac plexus or solar plexus is present on the anterior side of aorta around beginning of celiac trunk and Superior mesenteric artery, lies over the antero-lateral surface of aorta at T12/L1 vertebral level 						

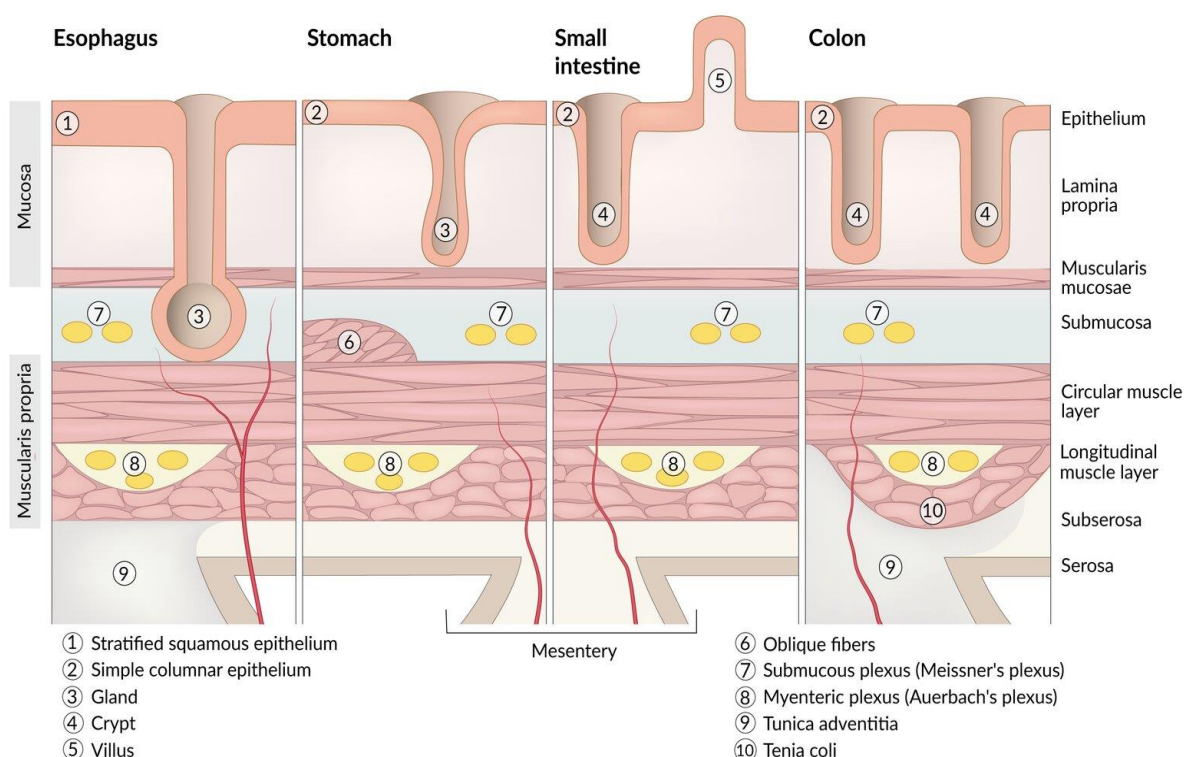
Clinical anatomy	Vagotomies	<ul style="list-style-type: none"> ❖ Truncal vagotomy reduces the maximal acid output by 50%, Decrease acid secretion + motility + dec in emptying. ❖ Highly selective Vagotomy: The unpleasant effect of surgery were largely avoided, although loss of receptive relaxation of the stomach did occur, leading to epigastric fullness and sometime mild dumping ❖ Thoracic vagotomy reduces gastric secretions
	Removal of stomach parts	<ul style="list-style-type: none"> ❖ Pylorus removal results in Increase in gastric emptying of solid or Solids pass easily. ❖ Antrum removal decreases gastrin because antrum contains G-cells (secrete gastrin) ❖ Fundus removal decreases compliance of stomach > Dec Receptive relaxation ❖ Effects of Gastrectomy ✚ Immediately → IDA occurs (due to low iron storage) ✚ After 3 months = iron deficiency anemia occurs ✚ Partial Gastrectomy → iron deficiency anemia occurs ✚ Total Gastrectomy. → B12 deficiency anemia occurs ✚ Overall : Iron Def anemia > B12 def ✚ Duodenum removal Increases in gastric emptying
	Jejunostomy Ileostomy Colostomy	<ul style="list-style-type: none"> ○ Complete Denervation of small intestine results in Paralytic ileus ○ jejunostomy or ileostomy Cause osmotic diarrhea. ○ jejunostomy + ileostomy Cause Secretory diarrhea. ○ Colostomy Causes secretory diarrhea. ○ serious complication of end colostomy is skin breakdown, cause hypokalaemia also.

FEATURE	SMALL INTESTINE	LARGE INTESTINE
Length	About 7 Meter Long	1.5 Meter Long Approx.
Calibre	Smaller	Larger
Motility	Freely mobile	Less mobile
Taenia coli (3 bands of longitudinal muscles)	Absent	Present
Sacculatation	Absent	Present
Appendices epiploic (fat)	Absent	Present over free surfaces of colon except caecum, appendix, and colon
Mucous membrane	Has permanent folds called Plica Semilunaris	No plica Semilunaris
Villi	Present	Absent
Payer patches	Present (in ileum), early typhoid infection here Microfold (M cells) Present in payer patches for Antigen presentation	Absent
Crypts of Lieberkühn (Glands)	Present in between villi, contain 2 types of cells: Paneth cell : rich in RER, secrete antimicrobial peptide, Zinc, and lysozyme. Goblet cell : mucous secretion	

DEODENUM	
Important Features	<ul style="list-style-type: none"> ○ C-shaped, shortest part of small intestine 10 inches/25cm length ○ Contains Submucosal glands (Bruner gland) ○ Demarcation of duodenum from jejunum is shown by ligament of Treitz. ○ The first 2cm of the superior (first) part of the duodenum Has a mesentery and is mobile. ○ The distal 3cm of the superior part and the other three parts of the duodenum have no mesentery. ○ and are immobile because they are retroperitoneal. ○ Superior part (1st part) is the Commonest site for peptic ulcer. ○ An ulcer of the posterior wall of the first part of the duodenum may penetrate the wall and erode the relatively large gastroduodenal artery, causing a severe hemorrhage. ○ Duodenum is the second most common site for diverticula in the gut. ○ Para duodenal recess (fossa) contains inferior mesenteric vein in its Free border edge. ○ Relations of 4 parts are summarized below; relation to SMA , SMV , AORTA ,IVC and Colon are imp
Blood supply	<ul style="list-style-type: none"> ○ Superior & inferior pancreaticoduodenal arteries, Rt Gastric & Rt Gastro-epiploic arteries ○ Superior pancreaticoduodenal is the main artery supplying 1st part Overall. ○ But initial 2cm of 1st part is supplied by Right gastric mainly. ○ others supplying first 2cm are Supradeodenal , paradeodenal , right gastroepiploic and least contribution to first 2cm by Superior pancreaticoduodenal artery (may even not supply 1st 2cm)
Venous drainage + lymphatics	<ul style="list-style-type: none"> ○ Venous drainage by SMV , splenic & portal vein ○ Lymph drains into Celiac & Super mesenteric nodes. ○ Ulcer of duodenum drains into CELIAC Nodes ; as 1st part is drained by celiac nodes mainly

Duodenum				
Part	Superior (1 st)	Descending (2 nd)	Inferior (3 rd)	Ascending (4 th)
Length	2 Inches	3 Inches	4 Inches	1 Inches
Level	L1 – transpyloric plane	L1 → L3	L3 – subcostal plane	L3 → L2
Relations	Anterior	1.Liver 2.Transverse colon 3.Small intestine (J & L)	1.Small intestine 2.Superior mesenteric vessels	Small intestine
	Posterior	1.Bile duct 2.Gastroduodenal artery 3.Portals vein	1.Right psoas major 2.Inferior vena cava 3.Abdominal aorta 4.Inferior mesenteric vessels	Left psoas major
	Medial	1.Pancreas		
	Lateral	1.Right colic flexure		

	JEJUNUM	ILEUM
LENGTH	Shorter (proximal 2/5)	Longer (distal 3/5)
DIAMETER	Wider	Narrower
WALL	Thicker (more plicae circulares)	Thinner (less plica circulares)
APPEARANCE	Dark red (more vascular)	Light red (less vascular)
VESSELS	Less arcades (long terminal branches)	More arcades (short terminal branches)
MESENTERIC FAT	Small amount near intestinal border	Large amount near intestinal border
LYMPHOID TISSUE	Few aggregations	Numerous aggregations (Peyer's patches)



Jejunum	<ul style="list-style-type: none"> wider bore, thicker walled, and redder than the ileum. Drains into superior mesenteric nodes. Supplied by greater and lesser splanchnic nerve. Feathery appearance on barium Recognized by single or double arcade arteries. Maximum absorption of water, Water + Electrolytes + folate occur in jejunum
Ileum	<ul style="list-style-type: none"> Most of the jejunum lies in left upper quadrant while ileum lies in right Lower quadrant. Terminal ileal resection causes: Increase water content of stool > Decrease Bile salt absorption > Decrease Vit-B12 absorption. Decrease turnover of chenodeoxycholic acid. The circular muscle of the lower end of the ileum (the ileocecal sphincter) serves as a sphincter and controls the flow of contents from the ileum into the colon.
Caecum & Appendix	<ul style="list-style-type: none"> Caecum lies on mesentery below ileocecal valve and retrocaecal fossa behind it 3 Taenia meet at the base of appendix The appendix lies in the right iliac fossa and Taenia coli are absent in appendix common position of appendix is Retrocecal. The Common type of intussusceptions is ileocolic.

	<ul style="list-style-type: none"> ○ McBurney's point: Situated 1/3rd of the way up the line joining the right anterior superior iliac spine to the Umbilicus. ○ Blood supply: Appendicular artery (usually a branch of inferior division of ileocolic artery) ○ The appendicular branch enters the free margin of and supplies the mesoappendix. ○ Lymph drainage via Superior Mesenteric lymph nodes ○ In Acute appendicitis Neutrophilic Leucocytosis is seen ○ Pain of pelvic appendix increase on flexing the thigh. ○ Appendicitis pain radiate to umbilicus through T-10 sympathetic. ○ During Appendectomy: Artery at risk of damage is Deep circumflex artery. ○ Nerve or structure at risk of damage is iliohypogastric nerve
Colon	<ul style="list-style-type: none"> ✚ Colon has 4 parts : Ascending, Transverse, Descending and Sigmoid colon ✚ Transverse Colon is the largest & mobile part of intestine. ✚ Ascending colon is Retroperitoneal , runs from ileocecal valve to hepatic flexure. ✚ Carcinoma of Right side (Asc colon) usually bleeds and causes iron def anemia. ✚ Carcinoma of left side (Descending colon) may cause Obstruction or altered bowel habits. ✚ Descending colon is Retroperitoneal , runs from splenic flexure to brim of pelvis. ✚ Sigmoid colon runs from Pelvic brim to S3 midline. ✚ Houston's valves are present in Rectum > Sigmoid Colon ✚ Splenic flexure is a common site of ischemia in bowel. ✚ Ileocecal Volvulus occurs in children while sigmoid volvulus more in old age (coffee bean sign) ✚ Nerve supply of Sigmoid colon is S2,S3, S4
Rectum	<ul style="list-style-type: none"> ✚ (13 cm) long, begins as continuation of Sigmoid colon Infront of S3 vertebrae. ✚ Sensitive to stretch. ✚ The puborectalis portion of the levator ani muscles forms a sling at the junction of the rectum with the anal canal and pulls this part of bowel forward, producing anorectal angle. ✚ The peritoneum covers the anterior and lateral surfaces of the first third of the rectum only. ✚ The anterior surface of the middle third, leaving the lower third devoid of peritoneum. ✚ The superior, middle, and inferior rectal arteries supply the rectum, sometimes Median sacral artery. ✚ The lymph vessels of the rectum drain first into the pararectal nodes and then into inferior Mesenteric nodes. ✚ Lymph vessels from lower rectum follow the middle rectal Artery to the internal iliac nodes. ✚ The nerve supply is from the sympathetic + parasympathetic nerves from inferior Hypogastric plexus
Anal sphincters	<ul style="list-style-type: none"> ✚ The internal sphincter is formed from a thickening of the smooth muscle of the circular coat at the upper end of the anal canal. ✚ The internal sphincter is enclosed by a sheath of striped muscle That forms the voluntary external sphincter. The external sphincter can be divided into three parts: <ol style="list-style-type: none"> 1. Subcutaneous part encircles lower end of anal canal and has no bony attachments. 2. Superficial part is attached to coccyx behind and perineal body in the front. 3. Deep part encircles the upper end of anal canal and has no bony Attachments.
Anorectal Ring	<ul style="list-style-type: none"> ✚ Formed by the fusion of Puborectalis + Deep external anal sphincter+ Internal anal sphincter. ✚ Ring is less marked where fibers of puborectalis are absent. ✚ Easily felt by a finger in the anal canal. ✚ Surgical division of this ring result in rectal incontinence
Anal Canal	<ul style="list-style-type: none"> ✚ 4cm long from Pelvic floor to outside ✚ 2 halves of 2cm each are separated by Dentate/ Pectinate Line ✚ 3 spongy mucosal cushions are in the Upper half at 3,7 & 11 'O Clock position contain capillary beds. ✚ They help with continence, air tightness & mucus production. ✚ Enlargement leads to haemorrhoids (piles) ✚ From the urethral group arise the Flock's and the Badenoch's arteries (both supply the transition zone). ✚ Flock's arteries approach the bladder neck at 2 and 10 o'clock. ✚ Badenoch's at 5 and 7'o clock

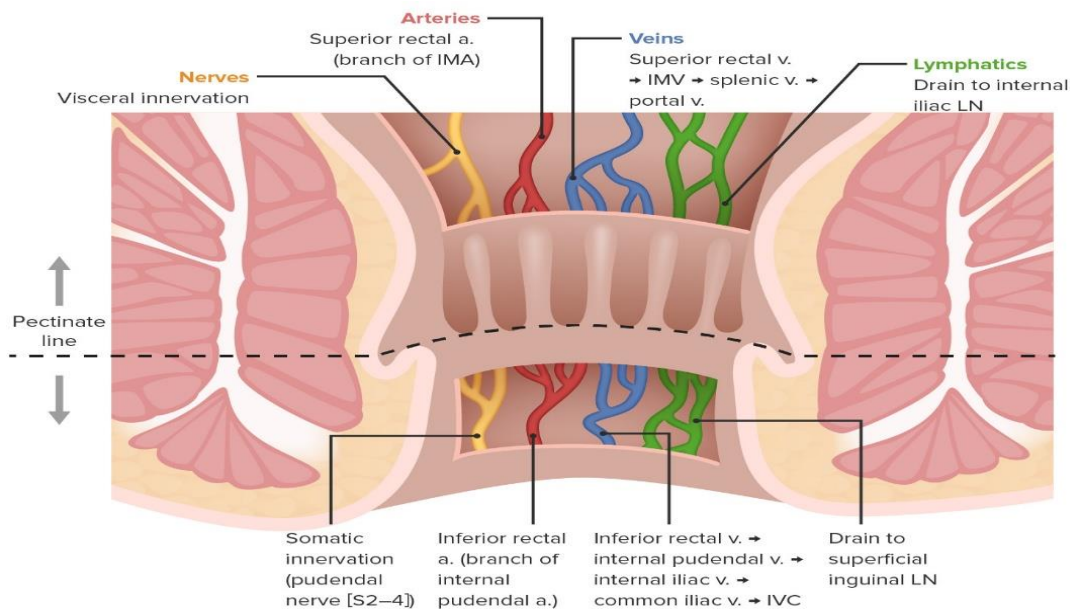
- ✚ **During Herniotomy:**
- ✓ structure at risk is Inferior epigastric artery, Nerve at risk is ilioinguinal nerve.
- ✚ Division of ilioinguinal never during appendectomy leads to direct inguinal hernia.
- ✚ Common / prominent structure encountered during inguinal hernia repair is Pampiniform plexus.

✚ Upper Half of Anal Canal

- ✚ Endoderm origin
- ✚ Columnar mucosa
- ✚ Columns, valves & cushions lining it.
- ✚ Autonomic nerves, insensitive to Touch
- ✚ Mainly superior rectal artery
- ✚ Portal venous drainage
- ✚ Internal iliac lymph nodes
- ✚ Adenocarcinoma
- ✚ Site of haemorrhoids

✚ Lower Half of Anal Canal

- ✚ Ectoderm origin
- ✚ Squamous mucosa
- ✚ Skin lining
- ✚ Somatic nerves, touch sensitive
- ✚ Mainly inferior rectal artery
- ✚ Systemic venous drainage
- ✚ Superficial inguinal nodes
- ✚ Squamous carcinoma
- ✚ No haemorrhoids



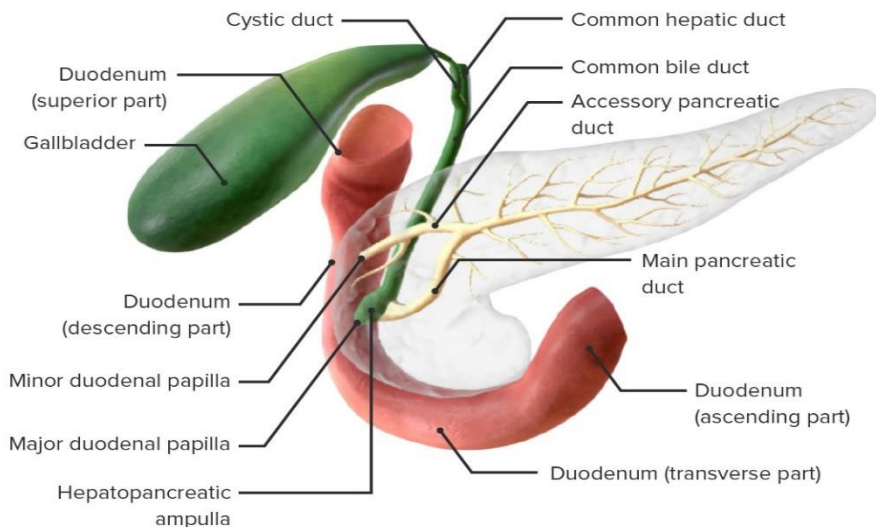
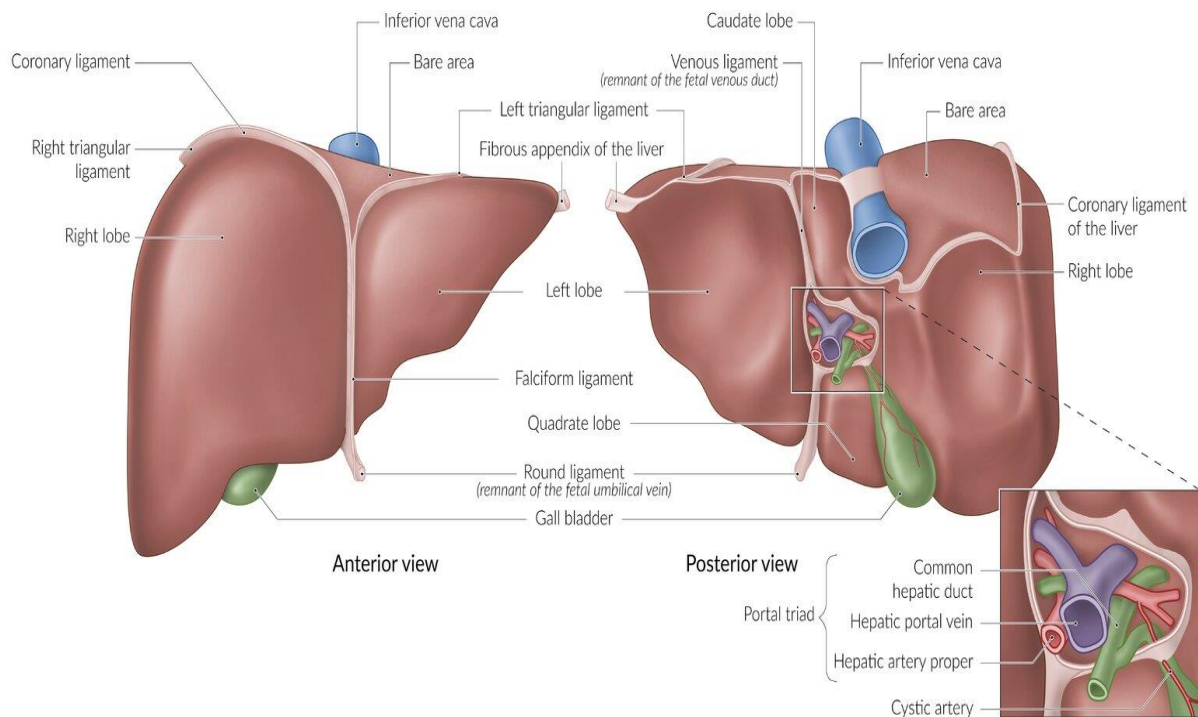
LIVER

General Features

- It is the largest gland of the body, weighing 1.5kg, wedge shaped, 1.5 Lit blood flow/min, 30% of CO. Capsule of liver is called Glisson capsule (a peritoneal membrane)
- Embryology, Liver develops from ventral mesentery of distal foregut
- Liver is 4% in fetus and 5% in newborn of total body wt. and occupy more space in Rt
- The liver is relatively much larger in the child than in the adult. In infant, the lower margin of the Liver extends inferiorly to a lower level than in the adult, this is an important consideration when making a diagnosis of hepatic enlargement
- Hepatic lobules are the Structural unit of liver while Hepatic Acinus is the Functional unit of liver
- Liver lies on Right- 6-10 ribs/costal cartilages and on Left-6-7 costal cartilages
- Surfaces: Anterior, superior, posterior, right, all are smooth except Postero-inferior (visceral) is concave
- Supports: IVC & hepatic veins (also ligamentum teres & peritoneum)
- Nerve supply: Right vagus via coeliac ganglia, left directly to porta hepatis.
- Eating a lot of pizza and burgers will cause Hypertrophy of Steatocytes
- Liver regenerate in 1-2week or 7-10 days by help of Hepatocyte Growth Factor (HGF)
- Liver pours bile into Space of DISSI. Liver has the least chance of infarction.
- liver is held in position in upper part of the abdominal by attachment of the hepatic veins to IVC

	<ul style="list-style-type: none"> ▪ Ito Cells Also known as “fat cell” or stellate cell Store vitamin A and During inflammation or liver damage, produce collagen, i.e., responsible for hepatic fibrosis/cirrhosis. ▪ volume of liver (80%) can be taken away safely because hepatocytes have great ability of regeneration.
Lobes of liver	<p>The division is made by the attachment of the Falciform ligament into two anatomical lobes.</p> <ul style="list-style-type: none"> ▪ Right lobe is the largest in volume and contributes to all surface of the liver and it is further divided into a quadrate lobe and a caudate lobe by gallbladder, the fissure for the ligamentum teres and IVC. ▪ Quadrate and caudate lobe are anatomical parts of right lobe but functional part of left lobe That’s why it is drained by left duct. ▪ Caudate lobe is situated between inferior vena cava and ligamentum venosum, received Blood from the left hepatic artery and drains bile into the left hepatic duct. ▪ Quadrate lobe is situated between gall bladder and groove for ligamentum teres, receives Blood from right and left hepatic artery and drains into both right and left hepatic duct. ▪ Left lobe is smaller. ▪ Cantlie’s line functionally divides liver into right and left liver, It extends between Gallbladder fossa and middle hepatic vein ▪ There are total 8 surgical lobes. Blood supply distinguish the surgical lobes by the bifurcation of the right and left hepatic artery and portal vein. Segmental division depends on portal vein
Supports of Liver	<ul style="list-style-type: none"> ▪ Hepatic veins-- main support, suspends liver from IVC and have no extrahepatic course ▪ Peritoneal folds, Surrounding organs, and Tone of anterior abdominal wall
Zones of Liver	<p>Zone I Peripheral zone: Affected 1st by viral hepatitis, richly supplied by blood, Ingested toxin metabolism occurs.</p> <p>Zone II intermediate zone: Affected by yellow fever.</p> <p>Zone III Pericentral vein (centrilobular) zone: Poorly oxygenated and more susceptible to hypoxia, affected 1st by ischemia Cytochrome p-450 metabolism occurs, most sensitive to metabolic toxins & It is the site of alcohol hepatitis</p>
Portal Triad	<p>BPH = Bile duct, Portal vein, Hepatic artery.</p> <p>(tumor located at Porta hepatis will most likely press branches of the portal Vein)</p>
Peritoneal ligaments of liver	<ul style="list-style-type: none"> ▪ Falciform ligament Is a two-layered fold of the peritoneum, ascends from the Umbilicus to the liver. ▪ It has a sickle-shaped free margin that contains the ligamentum teres, the remains of the Umbilical vein. ▪ We inject dye to liver through this ligament teres ▪ The Falciform ligament passes on anterior and superior surfaces of liver and splits into two layers. ▪ The right layer forms the upper layer of the coronary ligament ▪ The left layer forms the upper layer of the left triangular ligament. ▪ The right extremity of the coronary ligament is known as the right triangular ligament of liver ▪ Right triangular ligament is between the right lobe of the liver and diaphragm ▪ Left triangular ligament is between the left lobe of liver and diaphragm ▪ Coronary ligament is a triangular fold of the peritoneum attaching the naked area of the liver to the Diaphragm. It includes 2 layers- upper and lower that attach the liver to the diaphragm. ▪ Two peritoneal ligaments are a parts of the coronary Ligament ▪ Bare area of liver is limited by coronary ligament. ▪ The peritoneal layers forming the coronary ligament are widely Separated, leaving an area of liver devoid of peritoneum. Such an area is referred to as Bare area of the liver.
Blood supply	<ul style="list-style-type: none"> • Dual blood supply, Hepatic artery: Oxygenated blood flows in hepatic artery-25% • Portal vein: Nutrient rich blood flow through portal vein-75%

	<ul style="list-style-type: none"> blood drains from liver through 3 hepatic veins (right, middle Left) directly into the inferior vena cava.
Lymphatic drainage	<ul style="list-style-type: none"> Mainly into hepatic and celiac nodes. Liver produces large amount of lymph, about one third to one-half of all Body lymph. The lymph vessels leave the liver and enter the several lymph nodes in the porta Hepatis. The efferent vessels pass to the celiac nodes
Liver fetal circulation	<ul style="list-style-type: none"> Blood returns from the placenta via left umbilical vein which Joins the left branch of the portal vein. Most of the blood Crosses over into the ductus venosus and hence to the inferior Vena cava. Some blood enters the portal circulation and again Reaches the inferior vena cava via the hepatic veins
Hepatic veins	<ul style="list-style-type: none"> They drain cleansed blood back into the systemic Circulation from the liver. They do not follow the Porto-biliary segmentation and suspend liver from IVC helped by the peritoneal reflections
Gallbladder	<ul style="list-style-type: none"> Fibromuscular sac that stores and concentrates bile. Holds 50ml of bile Lined by simple columnar epithelium. Mucous cells at neck only Veins directly to liver bed then to hepatic veins. Occasionally join the portal vein Lymphatics to porta hepatis Parasympathetic & sympathetic same as liver Anteriorly liver and abdominal wall while posteriorly is transverse colon & 1st part of duodenum Fundus is under 9th costal cartilage in transpyloric plane Hartmann's pouch is an out-pouching of the wall of gallbladder at the junction of the neck of the gallbladder and the cystic duct This is not the feature of normal gallbladder and is always associated with pathological Condition and is the commonest site for impaction of gallstone
Calot's triangle	<ul style="list-style-type: none"> Aka as Hepatobiliary triangle: The space bounded by the cystic ducts inferiorly, the common hepatic duct medially and the Superior border of the cystic artery. It is an important surgical landmark as cystic artery can be found in its boundaries and must be identified by surgeon performing cholecystectomy to avoid Damage to the extrahepatic Biliary system
Bile duct & hepatic duct	<p>The right and left hepatic ducts emerge from the right and left lobes of the liver in the porta Hepatis. After a short course, the hepatic ducts unite to form the common hepatic duct</p> <p>The common hepatic duct is about 1.5 inch (4 cm) long and descends within the free margin of the lesser omentum. It is joined on right side by cystic duct from the gallbladder to form the bile duct</p> <p>Terminal end of CBD is embedded in the head of pancreas and that's why slow growing tumor of Head of pancreas will compress CBD</p> <p>Over 90% of bile duct cancers are Adenocarcinoma.</p> <p>The upper part of bile duct is provided by a twig from the descending branch of cystic Artery while its lower part is provided by the ascending branch of the superior Pancreaticoduodenal artery.</p> <p>Common bile duct divided into 4 parts:</p> <ol style="list-style-type: none"> Supradeodenal portion, upper 1/3rd part, 2 cm long, run in the free edge of lesser omentum Retroduodenal part (middle 1/3rd), posterior to 1st part of duodenum, right of portal vein + IVC Infraduodenal (or pancreatic) part: lower 1/3rd b/w head of pancreas and 2nd part of duodenum Intraduodenal part



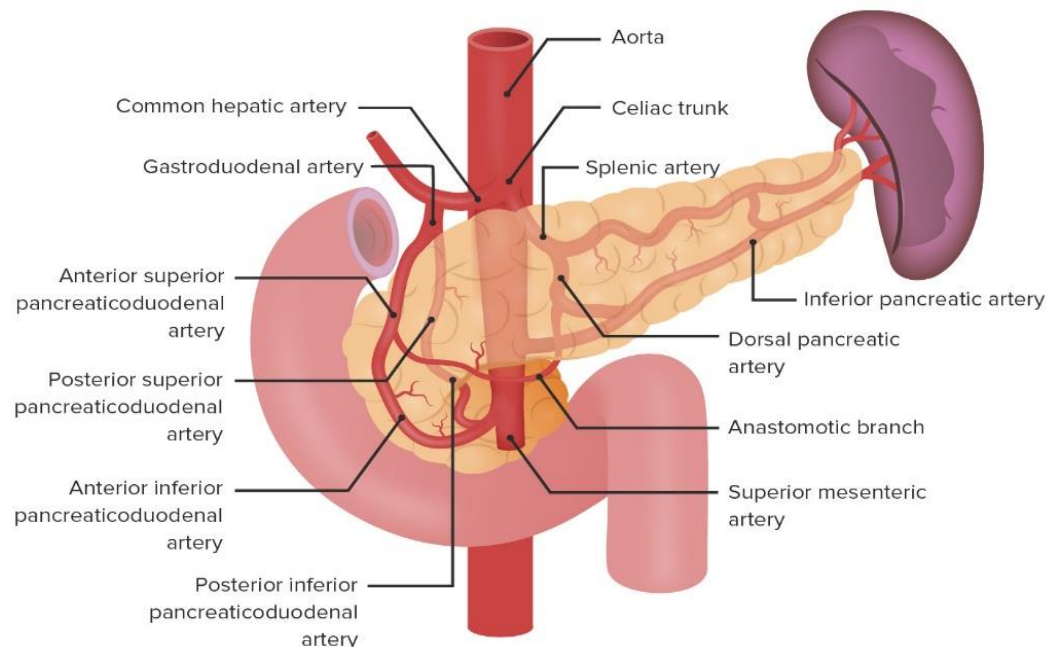
PANCREAS

- Entire ventral pancreatic duct forms main pancreatic duct
- Dorsal pancreatic duct Forms Uncinate process and portion of head of pancreas
- Proximal 1/3rd of dorsal bud degenerates and distal 2/3rd form pancreatic duct
- Exocrine volume of pancreas is much greater than endocrine.
- **Pancreas** Lies retroperitoneally, largely in the transpyloric plane.
- 15cm long, lobulated with fine capsule Alveoli of serous secretory cells lead to ductules then to principal Ducts
- Islets of Langerhans lie between alveoli

- Main duct (Wirsung) leads to ampulla of Vater, Accessory duct (Santorini) forms uncinata process, opens proximally
- Arteries: Gastroduodenal, inferior/superior pancreaticoduodenal, Arteria pancreatica magna from splenic artery
- Veins: Superior pancreaticoduodenal vein to portal vein, inferior pancreaticoduodenal to Superior mesenteric vein
- Lymphatics: in groove between head and duodenum and root of Superior mesenteric artery and vein
- Nerves: Parasympathetic (posterior vagus) to stimulate exocrine secretion
- Sympathetic for vasoconstriction and pain
- Secretions: Amylase. Secretin causes juice rich bicarbonate; Cholecystokinin causes juices rich in enzymes - trypsinogen, Chymotrypsinogen and pancreatic lipase
- Alpha islet cells give Glucagon, beta cells give insulin, delta give somatostatin. Pancreatic polypeptide is produced by the tail of the pancreas. Islets are abundant in TAIL of Pancreas & beta cells are 65% -- most abundant.
- **Annular pancreas** results due to failure of the ventral bud to rotate and elongates to encircle the upper part of the duodenum. Ventral pancreatic bud abnormally encircles 2nd part of duodenum, form a ring of Pancreatic tissue that causes duodenal narrowing and non-billous vomiting. Upper GI tract obstruction is the most common initial finding.
- **Accessory pancreas** Forms When the proximal 1/3rd don't regenerate and persists
- **Pancreatic divisum** results When distal 2/3rd of dorsal and entire ventral bud fail to fuse and distal one third persist thereby form two separate duct system

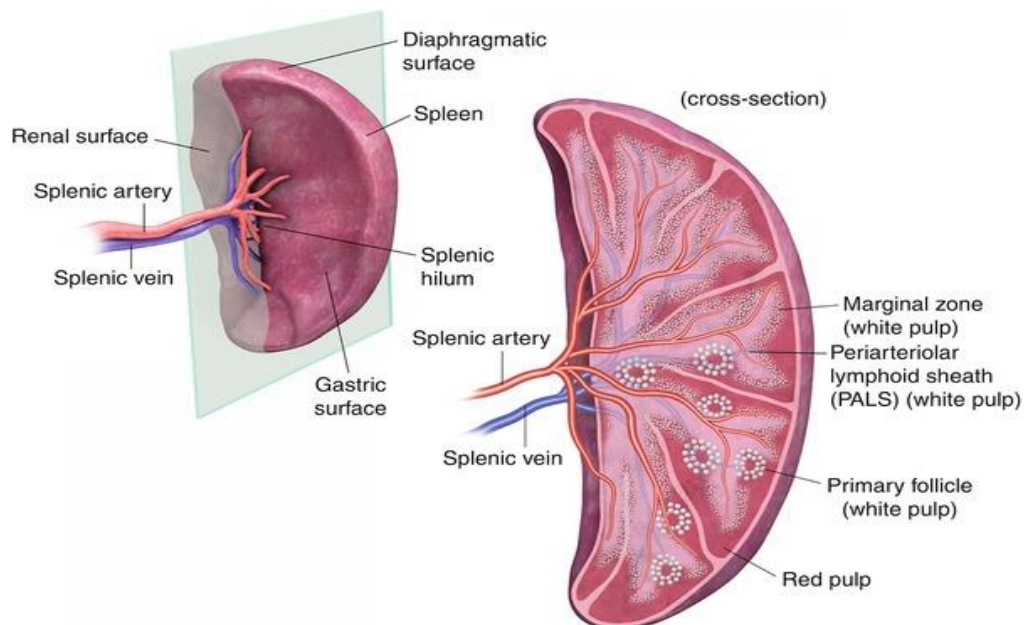
RELATIONS

- IVC is posterior to Head of pancreas. Posterior to neck Portal vein Begins at L2
- **Posterior to Body** are aorta and origin of SMA. Aorta is also posterior to Uncinate process
- **Anteriorly:** SMA+SMV arise at the lower border of pancreas and pass anterior to uncinata Process
- The splenic artery is the branch of celiac trunk and the primary source of blood
- **Superior pancreaticoduodenal artery is a branch of gastroduodenal artery.**
- **The inferior pancreaticoduodenal artery is a branch of SMA**



SPLEEN

- Arises from dorsal mesogastrium (Mesodermal origin).
- immunoglobulin synthesis occurs here by plasma cells.
- Largest lymphoid organ of the body, and, Part of the reticuloendothelial system.
- Becomes palpable when it is twice normal size and **enlarges towards RIF**
- Simple squamous epithelium (Peritoneum) covers the thin capsules of spleen
- Spleen has notch & moves on respiration. There is No Cortex or Medulla in Spleen.
- **Size of a fist , 200g in weight and lies on ribs 9-11**
- Functions: Erythropoiesis, effect erythrocyte removal, immune defence (beta cells) and blood storage
- Blood supply: Splenic artery from coeliac trunk and Venous drainage by Splenic vein to portal system
- **Lymph: Coeliac (para-aortic) nodes**
- Nerve: Sympathetic from coeliac plexus
- **Splenic infarction occur in CML and splenic rupture in infectious mononucleosis**
- **Streptococcus pneumonia is the most common cause of sepsis in Asplenic patient**
- **Spleen injury occur if 9th and 10th ribs fractured. Most common organ injured in Blunt trauma is spleen**
- **Spleen is least common site for malignancy**
- Wandering spleen: a rare condition in which there is absence or weakness of ligament that hold spleen in position
- **Accessory spleen if present found in the tail of pancreas.**
- Two forms exist, including the "sago spleen," in which amyloid deposits are limited to follicles, and the "lardaceous spleen," in which amyloid is deposited in the walls of the splenic sinusoids.
- Phrenicocolic ligament Prevents downward displacement of spleen
- Gastrosplenic ligament Extends from hilum of spleen to greater curvature of stomach and contains short gastric artery and left gastroepiploic artery
- **Splenorenal ligament (or lienorenal ligament) carries splenic vessels and tail of pancreas.**



KIDNEYS & SUPRA RENAL GLANDS

Features

- Kidney Wt. = 120g each, 11x6x4cm dimensions, 1200ml blood/minute and 1 million nephrons/kidney
- Retroperitoneal, moves 2.5cm on respiration. Pelvis faces medially/anterior.
- Lymphatics to para-aortic nodes at L2
- Sympathetic from T12-L1 causes vasoconstriction & pain.
- Parasympathetic from vagus. Function unknown
- Polar & capsular vessels give minimal collateral supply.
- Renal pyramids present in Medulla, but they are extensions of cortex (RMP)
- Medullary Rays are present Cortex (MRC). Minor calyces receive urine from RENAL PAPILLAE
- Capsule of kidney prevents spread of infection to Contralateral side > Lesser Sac.
- Renal medulla has collecting duct.
- Order of structures at HILUM = VAU (vein , artery , Ureter)
- Left renal vein is longer making Left nephrectomy easier.
- Rt Supra renal is Pyramidal in shape & Lt Supra Renal is Crescent shaped

Relations

- Right Kidney anteriorly Related to Liver
- Right Kidney Hilum Anteriorly Related to 2nd Part of Duodenum
- Posterior to Right Kidney lies 12th Rib & Diaphragm
- Anterior to Left Kidney are Stomach &, Pancreas
- Posterior to Left Kidney are 10th 11th Ribs & Diaphragm
- Anterior to Right Suprarenal gland are IVC and Right lobe of liver
- Posterior to Right Suprarenal gland -Diaphragm
- Anterior to Left Suprarenal gland are Pancreas , Lesser sac, and stomach
- Posterior to Left Suprarenal gland is Diaphragm

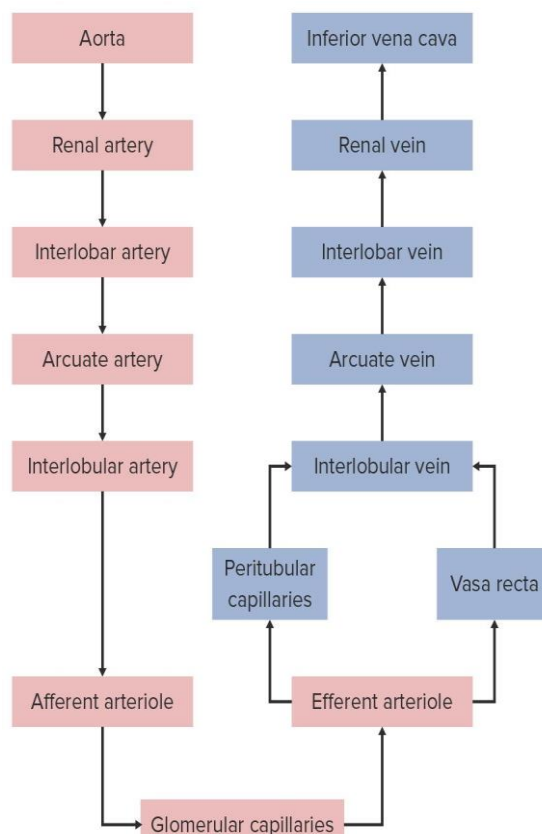
Key Facts

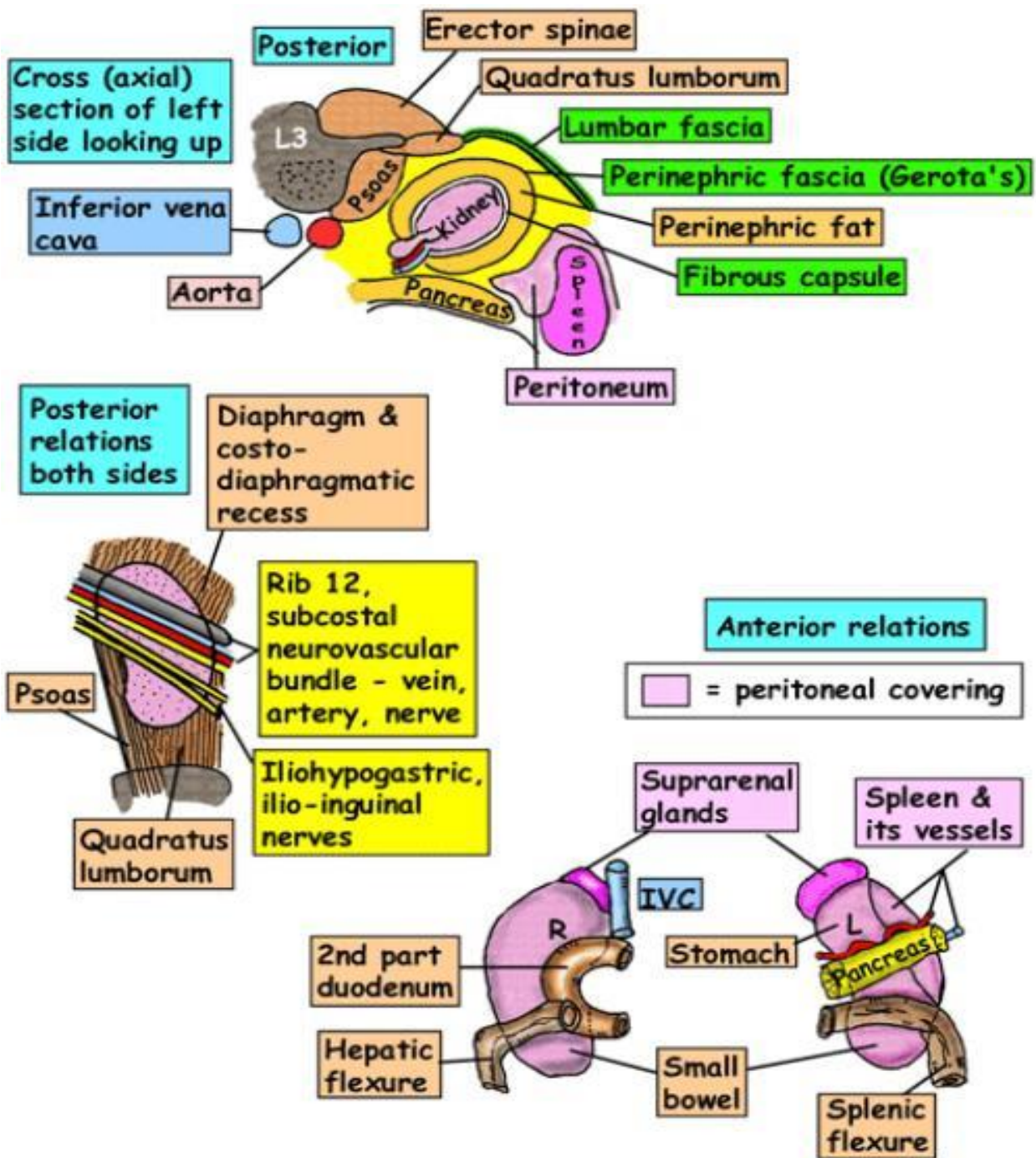
Sequence Of Vessels (Renal artery to Renal vein)

1. Renal Artery (branch of Abdominal aorta)
2. Segmental arteries
3. Inter lobar artery (Renal column has interlobar artery)
4. Arcuate artery (at base of pyramid)
5. Interlobular artery (capsule + glomerulus have it)
6. Afferent arterioles
7. Glomerular capillaries
8. Efferent arterioles
9. Peri tubular capillaries
10. interlobular veins
11. Arcuate vein
12. Interlobar vein
13. Renal Vein (drains into IVC)

Supra renal glands supplied by 3 arterial sources:

- Superior suprarenal artery from inferior phrenic artery
- middle suprarenal artery from abdominal aorta
- inferior suprarenal artery from Renal artery



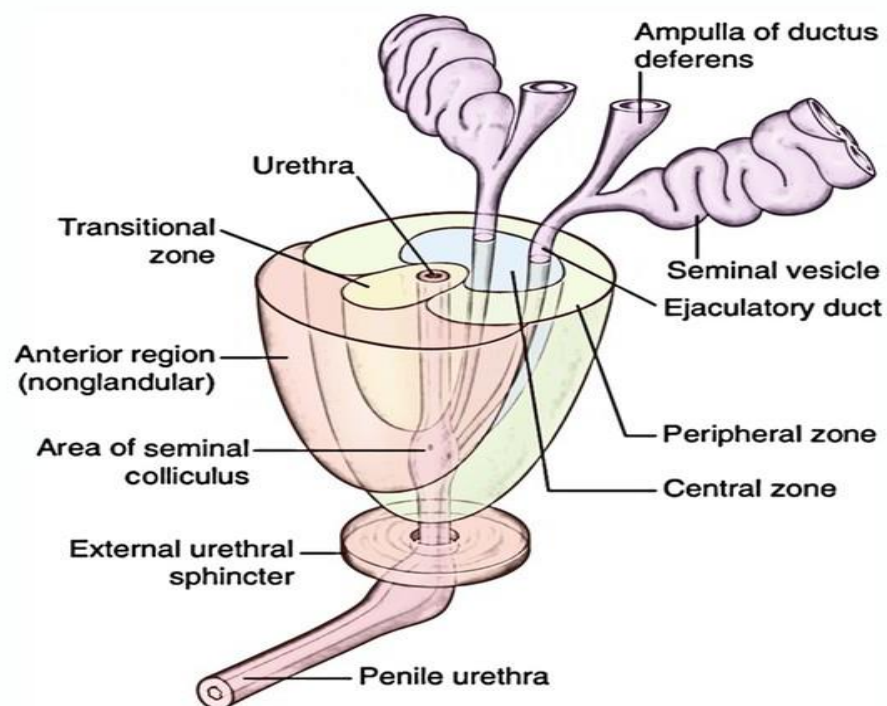
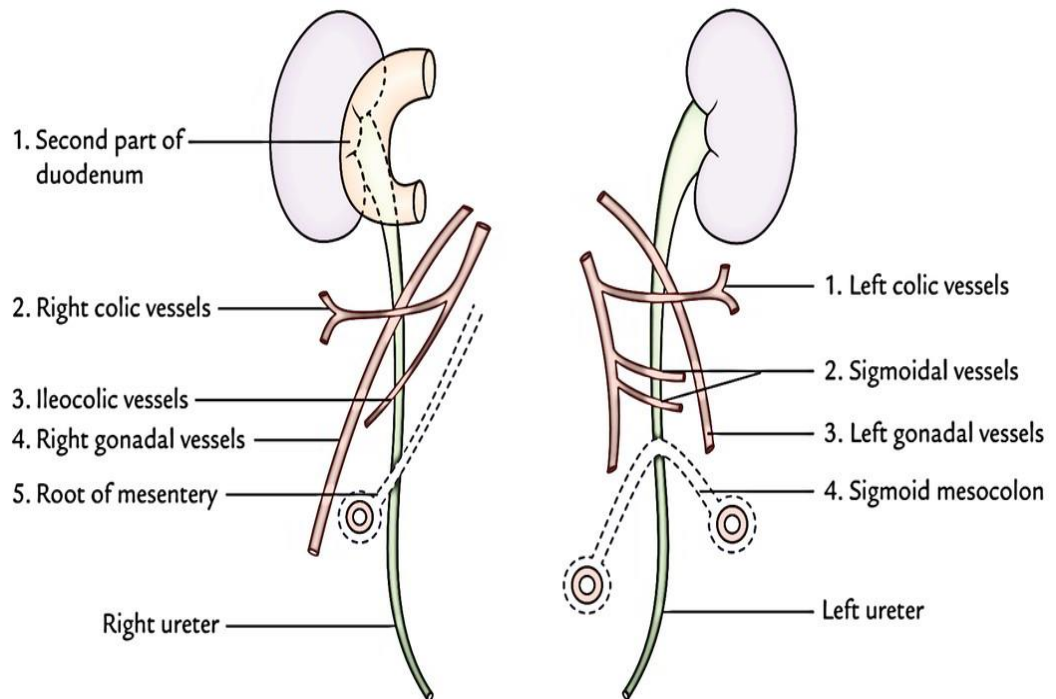


URETER	
Features	<ul style="list-style-type: none"> • 25cm long from kidney to bladder • It is recognisable as the most superficial structure in the pelvis Shows peristalsis • Posterior relations: Psoas, genitofemoral nerve, Sacroiliac joint, common iliac artery bifurcation • Anterior relations: <ul style="list-style-type: none"> • On Right: Duodenum, right Gonadal artery, right colic artery, ileal mesentery, Superior mesenteric artery. • On Left: Left gonadal Artery, left colic artery, sigmoid mesentery • Ureter Passes under: Vas deferens and uterine artery • It is Related to Lateral fornix of vagina in females (lateral to upper vagina) • Blood supply: Renal, gonadal, vesical, Branches from aorta, common iliac and vaginal Arteries • Nerves: General visceral afferents for pain and Sympathetic for vasoconstriction only • Pain is referred to loin, groin & tip of penis
Constrictions	<ul style="list-style-type: none"> • 3 main are : at Pelviureteric Junction, pelvic brim and ureterovesical junction
Course	<ul style="list-style-type: none"> • Sticks to the posterior surface of the peritoneum • Passes around the pelvic brim to 1cm short of the Ischial spine then swings medially • Enters the bladder at the level of the pubic Tubercle on a plain abdominal X-ray • Right ureter may be irritated by an inflamed appendix
Key Facts	<ul style="list-style-type: none"> • Location of Ureter injury during Hysterectomy: The Sequence is: • Cardinal Ligament > Broad Ligament > Pelvic Brim • During hysterectomy surgeon must know the relation of ureter along the base of broad ligament • Post hysterectomy pain is due to ligation of = ureter • Most common location of ureter damage in Oophorectomy is pelvic brim • During Hysterectomy Ureter damaged At Pelvic Brim in Relation To Uterine Artery • Ovarian artery crosses ureter at pelvic brim • Injury to suspensory ligament causes injury to ovarian vessels (these lie in suspensory ligament) • Cardinal ligament transmits uterine vessels. • Structure damaged behind ovarian fossa is Ureter > Internal iliac artery. • Vessel damaged behind ovarian fossa is Internal iliac artery. • Investigation to detect ureteral injury is IV pyelogram
BLADDER	
Key features	<ul style="list-style-type: none"> ▪ Transitional epithelium, Rubbery, watertight, lax, stretchy, No glands ▪ Trigone is derived from Mesoderm. Transitional epithelium is derived from Endoderm. ▪ Bladder epithelium derived from Endoderm + Mesoderm. ▪ Kidney epithelium derived from = Endoderm + mesoderm , nephron from mesoderm ▪ urethra epithelium from Endoderm. Terminal urethra epithelium is from ectoderm source. ▪ Alpha receptors are abundant at neck of bladder & proximal urethra. ▪ Muscle: Whorls of smooth muscles, detrusor, 3 layers (Inner & outer longitudinal, middle circular) ▪ Arteries: Superior/inferior vesical, obturator, inferior Uterine, vaginal artery supply ▪ Veins converge to vesicoprostatic plexus in males, plexus at base of broad ligament in female, it finally drains into the internal iliac. ▪ Lymphatics: Internal and external iliac nodes ▪ Nerves: Sympathetic (male only at bladder neck) closes bladder Neck at ejaculation. Inhibitory, vasomotor, carries pain in both sexes. ▪ Parasympathetic – motor to detrusor, sensory for full Bladder, some pain, autonomic stretch reflex in infants, later modified by cortical inhibition ▪ Relations on Posterior View : From LATERAL TO MEDIAL ▪ MNEMONICS = USA → Ureter , seminal vesicles, ampulla of vas deferens ▪ Inferior epigastric artery may be injured while doing Supra pubic catheterization.

PROSTATE	
Features	<ul style="list-style-type: none"> Fibromuscular gland having abundant stroma containing smooth muscles. Pyramidal shape with posterior groove, Size of chestnut (2 x 3 x 4cm), Sits on UG diaphragm. weight = 18gm. Intrinsic urethral mechanism around it and urethra runs through it. Apex is the most inferior part of it. Prostate gives nutrients for sperms and contributes the 30 % of the ejaculate volume. Ejaculatory ducts & prostatic utricle (paramesonephric remnant) open onto Verumontanum in floor of prostatic urethra. Prostate has a True and false capsule. Denonviller's fascia/ Rectovesical fascia are fused layers of peritoneum present posterior to bladder on prostate. This fascial layer must be preserved in prostatectomy, otherwise Rectourethral fistula may form. Veins: Preprostatic plexus, valveless (to vertebral plexuses) -- route of Metastasis of Ca prostate to Vertebrae Arteries: Inferior vesical, middle rectal, internal pudendal Nerves: Sympathetic for ejaculation & smooth muscle contraction Parasympathetic for erection & secretomotor to acini The old surgical view of the prostate consisted of three lobes Anterior lobe, Middle lobe, and Posterior lobe (lateral extensions of which gave lateral lobes Which were only significant if the prostate Was hypertrophied) Modern zonal view suggests that the lobes Are arranged in zones Transitional zone: surrounds the Urethra. Liable to BPH (stroma & glandular enlargement) Central Zone : surrounds ejaculatory duct all the way to Verumontum Peripheral zone: surrounds the Other two zones. 70% of cancers Start here. It is pushed peripherally by benign enlargement and compressed
Imp facts	<p>In BPH, Transitional Zone or Median Lobe involved</p> <p>In Carcinoma prostate : Peripheral Zone / Posterior Lobe involved.</p> <p>Median lobe is structurally largest while Lateral lobe is anatomically largest.</p> <p>Peripheral zone is the largest zone.</p> <p>PSA is not sensitive indicator of Prostate Cancer but can be used for Screening and Follow Up</p> <p>Hard irregular, firm mass or nodule on DRE indicates cancer.</p> <p>In BPH, Smooth symmetrical nodular enlargement occurs.</p> <p>Gleason's scoring is done for prostate cancer staging & prognosis.</p> <p>In prostate cancer –bone metastasis occurs leading to raised ALP.</p> <p>Dihydrotestosterone (DHT) is involved in BPH pathogenesis</p>
URETHRA & PENIS	
Features	<p>Anterior and Posterior Urethra.</p> <p>Posterior Urethra = Prostatic urethra approximately 2.5cm + Membranous urethra 2cm</p> <p>Anterior Urethra = Bulbous + Penile or pendulous make the anterior urethra. Approximately 20cm</p> <p>Spongy part of male urethra located at Glans penis is called NAVICULAR FOSSA</p> <p>LEAST dilatable part of Urethra is MEMBRANOUS Urethra</p> <p>Narrowest part of Urethra is EXTERNAL Urethral Meatus</p> <p>Widest / Most dilated part of urethra is PROSTATIC Urethra</p> <p>Blood supply:</p> <p>Artery to bulb to glans & corpus spongiosum & Deep artery of penis to corpus cavernosum</p> <p>Dorsal artery of penis to skin, fascia, glans penis, Urethral artery from dorsal artery</p> <p>Veins: Superficial & deep dorsal veins of penis</p> <p>Lymph: Skin to superficial inguinal nodes. Glans, corpora, and urethra to deep inguinal nodes</p> <p>Nerves: Posterior scrotal n to skin & glans. Pudendal gives dorsal nerve of penis.</p> <p>Sympathetic for emission while Parasympathetic to corpora for erection</p> <p>Pudendal nerve for ejaculation (both somatic & visceral)</p> <p>Receives: Ejaculatory ducts, bulbourethral glands, urethral glands</p>

Clinical anatomy

- Rupture of membranous urethra : urine extravasate into deep perineal pouch (MUD)
- Rupture of bulbar urethra : urine leaks into superficial perineal pouch (BUS)
- Rupture of penile urethra : urine leaks into scrotum and then ant abdominal wall (PUS)
- Injury to penile urethra causes urine to leak into : perineum, scrotum + anterior Abd wall
- After a bicycle injury/ fall, urine extends upto abdomen but not thigh in penile urethra rupture

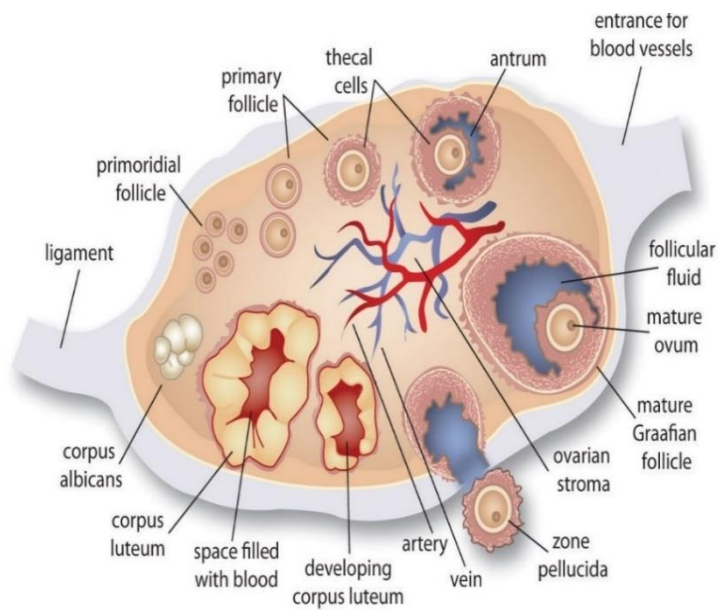
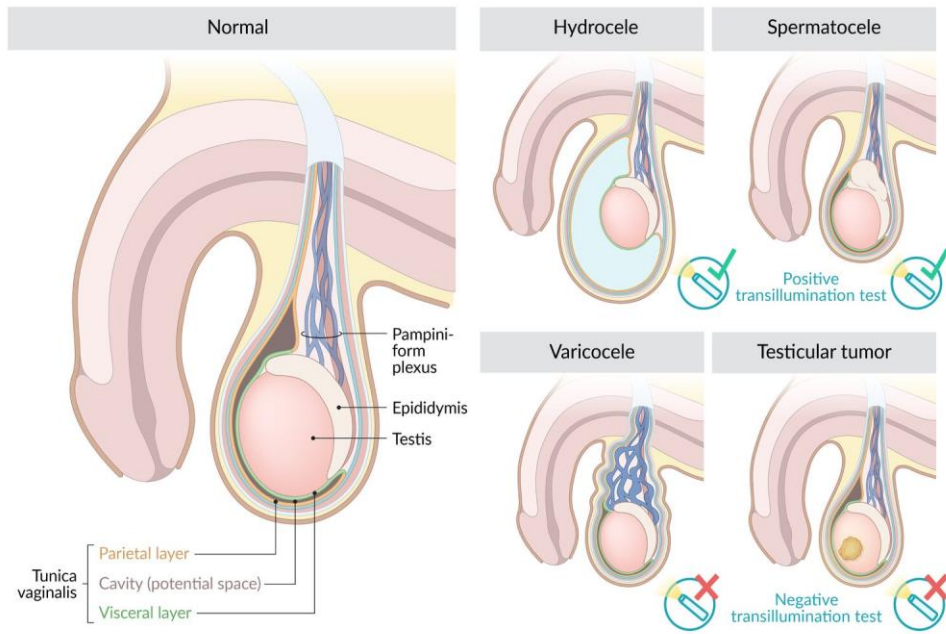


Seminal vesicles	<ul style="list-style-type: none"> Inferiorly each seminal vesicle narrows and joins the vas deferens of same side and form the ejaculatory duct. Lined by Pseudo stratified Columnar Epithelium Functions: Secrete yellow fluid containing Fructose , PGs, and Vit C Seminal vesicles fluid constitutes 70% of ejaculate. After Vasectomy Seminal fluid consists of Seminal fluid + Prostatic fluid
Epididymis	<ul style="list-style-type: none"> Divided into three regions: the caput, the corpus, and the Cauda epididymis. Epididymis serves to: transport sperm, store it, increase fertility, and promote motility + maturation. Epididymis function is temperature and androgen (DHT) dependent. Fertility maturation is achieved at the level of the late corpus or early cauda epididymis
Ductus deferens	<ul style="list-style-type: none"> Terminal part of the vas deferens is dilated to form the ampulla of the vasa deferens The inferior end of ampulla narrows down and joins the duct of seminal vesicle to form the ejaculatory duct. It passes lateral to inferior Epigastric artery, in inguinal ring at deep ring and cross ureter in the region of ischial spine. Pseudostratified columnar epithelium with Thick three layers of smooth muscle coats: inner, outer, longitudinal, and middle circular layer Function: Delivers Spermatozoa from tail of Epididymis to the ejaculatory duct
Ejaculatory duct	<ul style="list-style-type: none"> Formed by the union of the vas deferens and the duct of seminal vesicle Epithelium: Simple columnar epithelium. It lacks a muscular wall. Function: Delivers spermatozoa, seminal fluid to the prostatic urethra at colliculus seminalis.
Blood supply & lymphatic drainage	<p>Prostate + Seminal Vesicle + Vas deferens + Ejaculatory duct :</p> <ul style="list-style-type: none"> All supplied by inferior Vesical & Middle rectal artery. Internal iliac vein drains all these. Inter Iliac nodes are the main lymphatics route of all these above-mentioned structures.

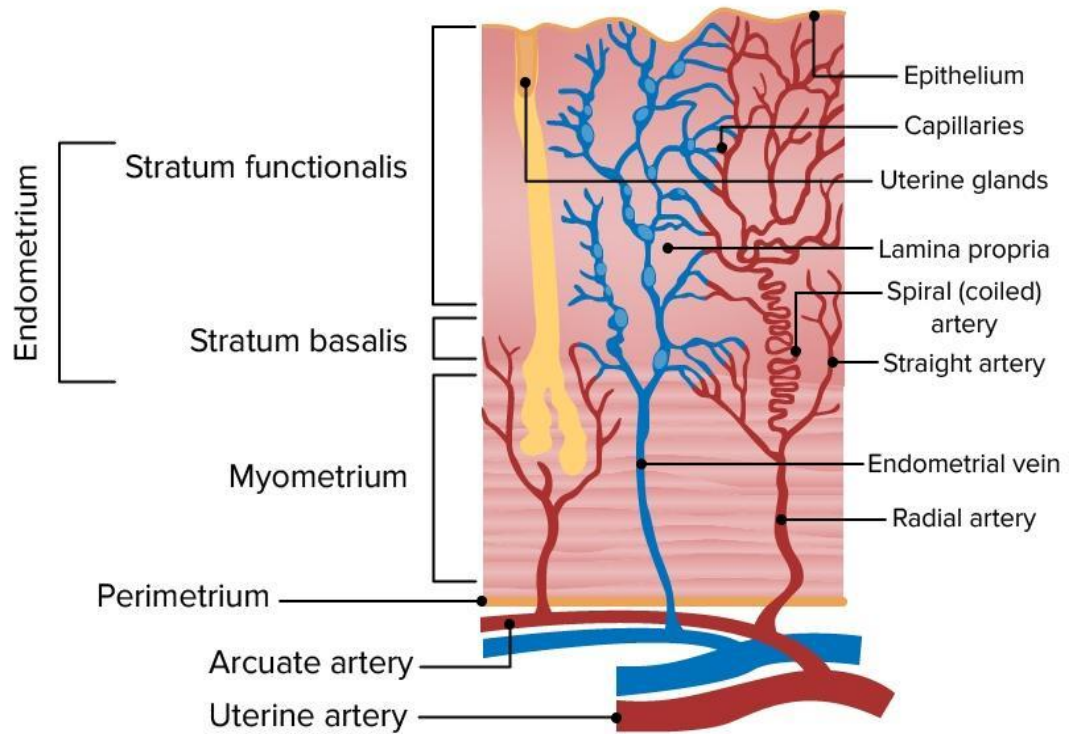
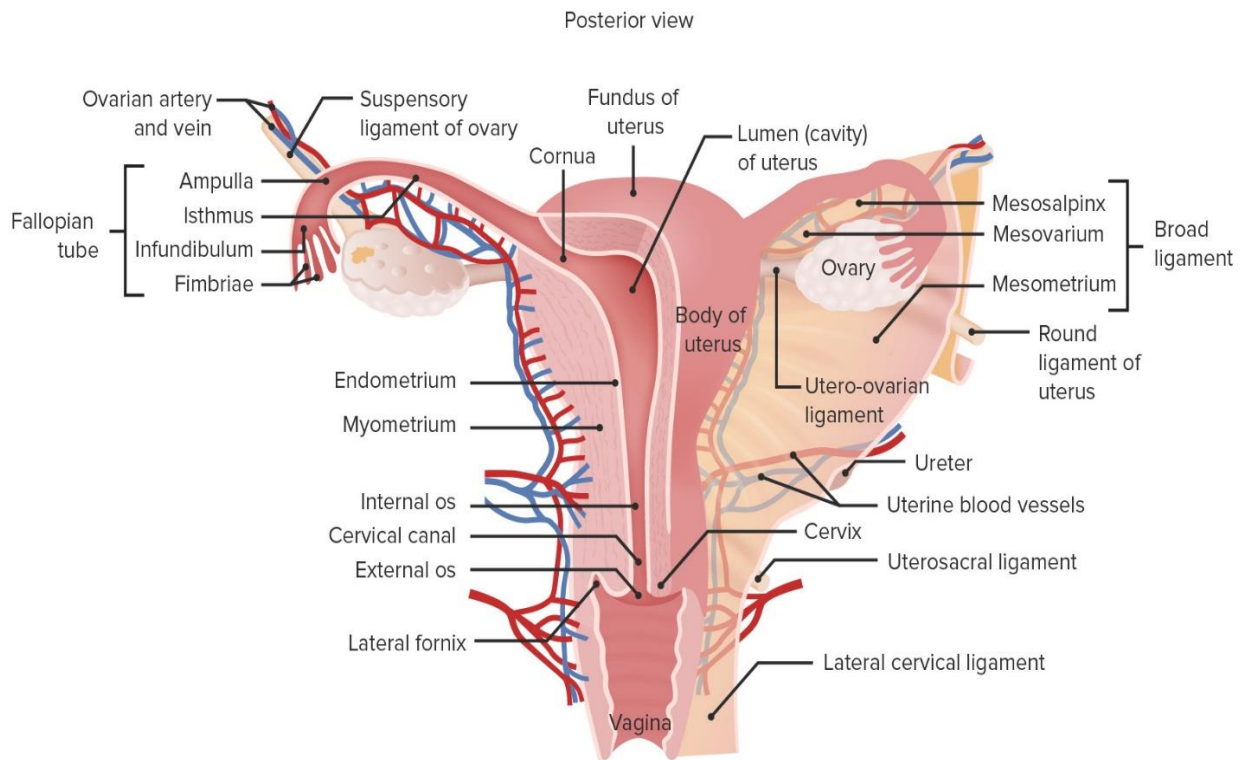
TESTES

General features	<ul style="list-style-type: none"> Position in the scrotum: The testis is suspended in the scrotum by the spermatic cord. It is located obliquely, so that its upper pole is leaned somewhat forwards and laterally, and lower pole backward and medially. The innermost layer is tunica Vasculosa. The testes are normally 6 cm in length and 4 cm in width. Testis volume is generally above 16 ml and averages 20 ml. In humans, interstitial tissue takes up 20% to 30% of the total testicular volume whereas germ line cells constitute the remainder (70%- 80%).
Blood supply	<ul style="list-style-type: none"> Arterial supply by testicular artery. Venous drainage via Pampiniform plexus. The Pampiniform plexus of veins forms from the internal spermatic or gonadal veins. These veins are spared during Varicocele ligation surgery.
Lymphatics	<ul style="list-style-type: none"> Drain into bilateral pre-aortic and a para-aortic groups of lymph nodes
Clinical anatomy	<ul style="list-style-type: none"> Hydrocele : Fluid accumulates in Tunica Vaginalis (derived from Parietal Peritoneum) Undescended Testis / Cryptorchidism: inc Risk of Cancer > infertility, must be treated before 1 year of age. Varicocele: Dilatation of Pampiniform venous plexus, Mostly Left sided ; as Left renal vein may be compressed by Transverse colon and has a straighter course than right vein Testicular Torsion: An emergency occurs commonly in sleep / Playing and must be treated in 6 hrs.

SCROTUM	
Layers	<ul style="list-style-type: none"> • Superficial fascia: the Dartos muscle (smooth muscle) replaces the fatty layer. • Anterior abdominal wall, and Scarpa's fascia (membranous layer) is now called Colles' fascia. • External spermatic fascia derived from the external oblique • Cremasteric fascia derived from the internal oblique • Internal spermatic fascia derived from the fascia transversalis • Tunica vaginalis, which is a closed sac that covers the anterior, medial, and lateral surfaces of it
Nerve supply	<ul style="list-style-type: none"> • Anterior surface: main -- ilioinguinal nerves + small contribution by genital branch of Genitofemoral nerve • Posterior surface: by branches of perineal nerves and posterior Cutaneous nerves of the thigh.
Blood supply	The external pudendal branches of the femoral and scrotal branches of the internal Pudendal arteries supply the scrotum. The veins accompany the corresponding arteries.
Lymphatics	The wall of the scrotum is drained into the medial group of superficial inguinal lymph nodes
Clinical anatomy	<ul style="list-style-type: none"> • Hydrocele is the Painless collection of Fluid inside tunica Vaginalis • while aspirating fluid the needle should not pierce tunica albuginea. • Transillumination test is +ve in Hydrocele while -ve in the Haematocele/ pus/lymph collection. • Inner most layer of scrotum is TUNICA VASCULOSA , NOT tunica albuginea • Patent processes vaginalis is linked to Indirect inguinal hernia and cryptorchidism in children
OVARY	
Features and relations	<ul style="list-style-type: none"> • The ovaries are located in the ovarian fossa on the lateral pelvic wall below the pelvic brim • A negligible peritoneal depression is the ovarian fossa which is also surrounded Posteriorly by the ureter > internal iliac vessels while Anteriorly by the external iliac vessels. • Inferiorly by the uterine tubes (in the complimentary margin of the broad ligament) • innervated by the postganglionic sympathetic (T10, T11) and parasympathetic (S2- S4)
Blood supply	<ul style="list-style-type: none"> • Arterial supply: ovarian artery, which originates from aorta at the level of L1 • Venous drainage: pampiniform plexus around the ovarian artery, from which a single ovarian vein is composed near the superior aperture of the pelvis/pelvic inlet. • right ovarian vein empties into IVC while the left ovarian vein empties into the left renal vein.
Lymphatics	<ul style="list-style-type: none"> • drain into the pre-aortic and bilateral para-aortic lymph nodes
Clinical correlations	<ul style="list-style-type: none"> • Red Degeneration of ovarian cyst may occur in Pregnancy leading to Acute Abdomen • Polycystic ovaries are associated with Risk of Type 2 DM , Insulin Resistance & IHD • In Polycystic ovaries : ratio of LH:FSH = 3:1. • polycystic ovarian syndrome has triad of: Oligo menorrhea + Hirsutism and acne + Obesity or weight Gain. Cystic ovaries on USG Metformin can be used in PCOS in insulin resistance. Cyproterone acetate for Acne OCPs are also helpful, Laser therapy for Hirsutism. Lifestyle modifications carry importance.



UTERUS	
Features	<ul style="list-style-type: none"> ○ Pear shaped, usually anteverted to 90 degrees, and, anteflexed to 170 degrees ○ Has no submucosa. ○ Histology – Cervix: Tall columnar epithelium becoming squamous Outside, alkaline mucus ○ Rest of uterus: Endometrium with glands, arterioles, Smooth whorls of muscle, columnar epithelium ○ <u>Wall of uterus is made of 3 layers:</u> ○ Perimetrium (thin outer layer), Myometrium (thick smooth muscle layer), and, Endometrium (innermost) ○ <u>Endometrium has two layers:</u> ● Basal layer: adjacent to myometrium, regenerates after each cycle and is not sloughed off ● Functional layer: provide a proper site for implantation, shed, or lost during menstruation because of ischemic necrosis due to Withdrawal of estrogen and progesterone Functional layer consists of compact and spongy layer and shed at menstruation and parturition ● Compact layer: thin and superficial layer and consist of densely packed Stromal cells ● Spongy layer: thick, composed of oedematous stroma (contains dilated tortuous uterine gland)
Relations	<ul style="list-style-type: none"> ● Anterior: vesicouterine pouch, posterior/superior bladder, Anterior fornix, small bowel ● Posterior- Pouch of Douglas, ileum, sigmoid ● Lateral: Uterine vessels, ureter, lateral fornix, broad Ligament
Supports of uterus	<ul style="list-style-type: none"> ➤ Passive support: By Ligaments that are condensations of Pelvic fascia (e.g. , Cardinal ligament) ➤ Active/dynamic support: Pelvic diaphragm made of levator ani muscle ➤ Main support of pelvic Organs is Pelvic diaphragm ● Cardinal ligament or Mackenrodt's ligament or Transverse cervical ligament: It is the condensation of pelvic fascia that pass to the cervix and upper end of the vagina from the lateral wall of the pelvis. It can be Palpated on pelvic exam. It is the Strongest ligament, provides Major support to the uterus + prevents Uterine prolapse. Uterus remain in position (Anteverted & Anteflexed) by this ligament It is Injured during uterovaginal Prolapse ● Sacro-cervical ligament or Uterosacral Ligament (involved in 1st, 2nd, 3rd degree uterine prolapse) ● Pubo-cervical ligament
Uterine prolapse	<ul style="list-style-type: none"> ● Stage I – the uterus is in the upper half of the vagina. ● Stage II – the uterus has descended nearly to the opening (Os) of the vagina. ● Stage III – the uterus protrudes out of the vagina. ● Stage IV – the uterus is completely out of the vagina ● Ligaments involved in 1st – 3rd degree Prolapse is uterosacral ● In 4th degree prolapse (procidentia) -- cardinal ligament involved
Blood + Nerve supply	<p>Blood supply via Uterine + Ovarian arteries</p> <p>Venous drainage: mainly by internal iliac vein via Highly plexiform to vesical and rectal plexuses</p> <p>Nerves – Motor: Parasympathetic activate muscle, Sympathetic relax muscle. Both from pelvic plexus. Sensory: Parasympathetic for cervix & Sympathetic for uterus</p>
Lymphatic drainage	<ul style="list-style-type: none"> ● Fundus : Para -aortic nodes at L1 ; Lymphatics accompany the ovarian artery ● Body + Cervix : drain into the internal and external iliac lymph node ● few lymph vessels follow the round ligament of the uterus through the inguinal canal and drain into the superficial inguinal lymph nodes ● Uterine cancer spreads to labia majora by round ligament of uterus ● Round ligament of uterus is both intra + extra peritoneal ● Gubernaculum derivative in female is round ligament of uterus and round ligament of ovary.

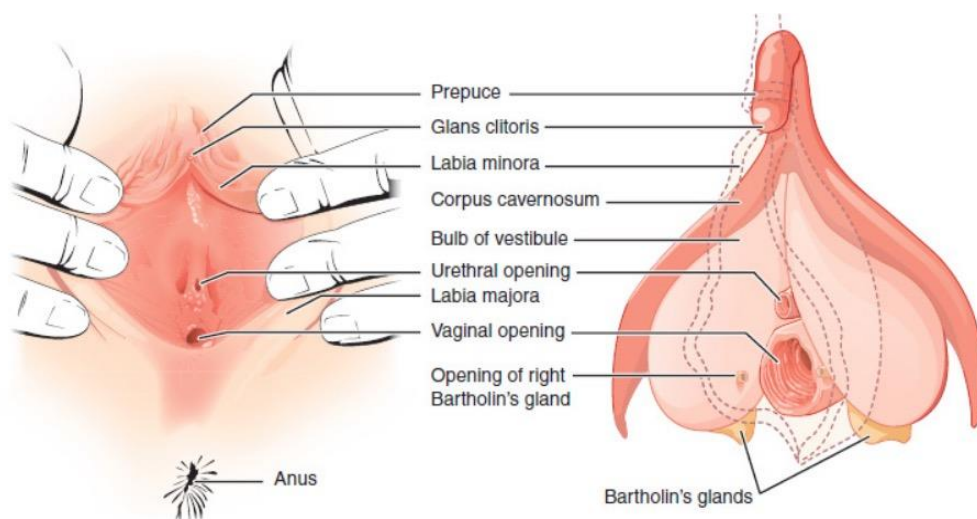


Broad ligament of Ovary	<p>Flat sheet of the peritoneum, associated with the uterus, fallopian tubes and ovaries extending from the lateral pelvic walls on both sides and folds over the internal female genitalia, covering their surface anteriorly and posteriorly.</p> <p>It prevents ovaries from falling .</p> <p>The ovary is kept in position by the broad ligament and the Mesovarium</p> <p>Anatomically divided into three regions or Subdivisions :</p> <ul style="list-style-type: none"> • Mesometrium: Surrounds the uterus and is the largest subsection of the broad ligament, encloses the proximal part of the round ligament of the uterus. • Mesovarium: attaches to the hilum of the ovary, enclosing its neurovascular supply. It does not, however, cover the surface of the ovary itself. • Mesosalphinx enclosing the fallopian tubes. <p><u>Relations of Broad ligament</u></p> <ul style="list-style-type: none"> • It is attached to the uterus, fallopian tubes, and ovaries. These organs are supplied by the ovarian and uterine arteries, which are also contained within the broad ligament. • Three other ligaments of the female reproductive tract are located within the broad ligament: Ovarian ligament, round ligament of uterus, Suspensory ligament of ovary. • After pregnancy, the broad ligament is lax, and the ovary may prolapse into the Rectouterine pouch. The ovary may be tender and cause discomfort on intercourse
Ovarian ligament	<ul style="list-style-type: none"> • Attached to the ovary inferiorly, thus, connects the ovary to the side of the uterus. • It joins the uterus just below the origin of the fallopian tubes. • Structurally, it is a fibrous band of tissue that lies within the broad ligament.
Suspensory ligament of Ovary	<ul style="list-style-type: none"> • Aka Infundibulopelvic ligament • Extends outwards from the ovary to the lateral abdominal wall • It consists of fold of peritoneum (some consider it to be part of the broad ligament) • The function of this ligament is to contain the ovarian vessels and nerves (ovarian artery, ovarian vein, ovarian nerve plexus and lymphatic vessels).
Round ligament of Uterus	<ul style="list-style-type: none"> • Extends from Superolateral angle of uterus and pass through deep and superficial inguinal ring to attach or terminate on labium majora • Both intra-pelvic and extra-pelvic course • keeps the uterus anteverted and anteflexed , not palpated on pelvic exam • prevents uterus from falling down and considerably stretches during pregnancy • Carcinoma uterus and cervix spreads to labia majora via round ligament of uterus • The round ligament is a remnant of the embryonic Gubernaculum.

KEY FACTS

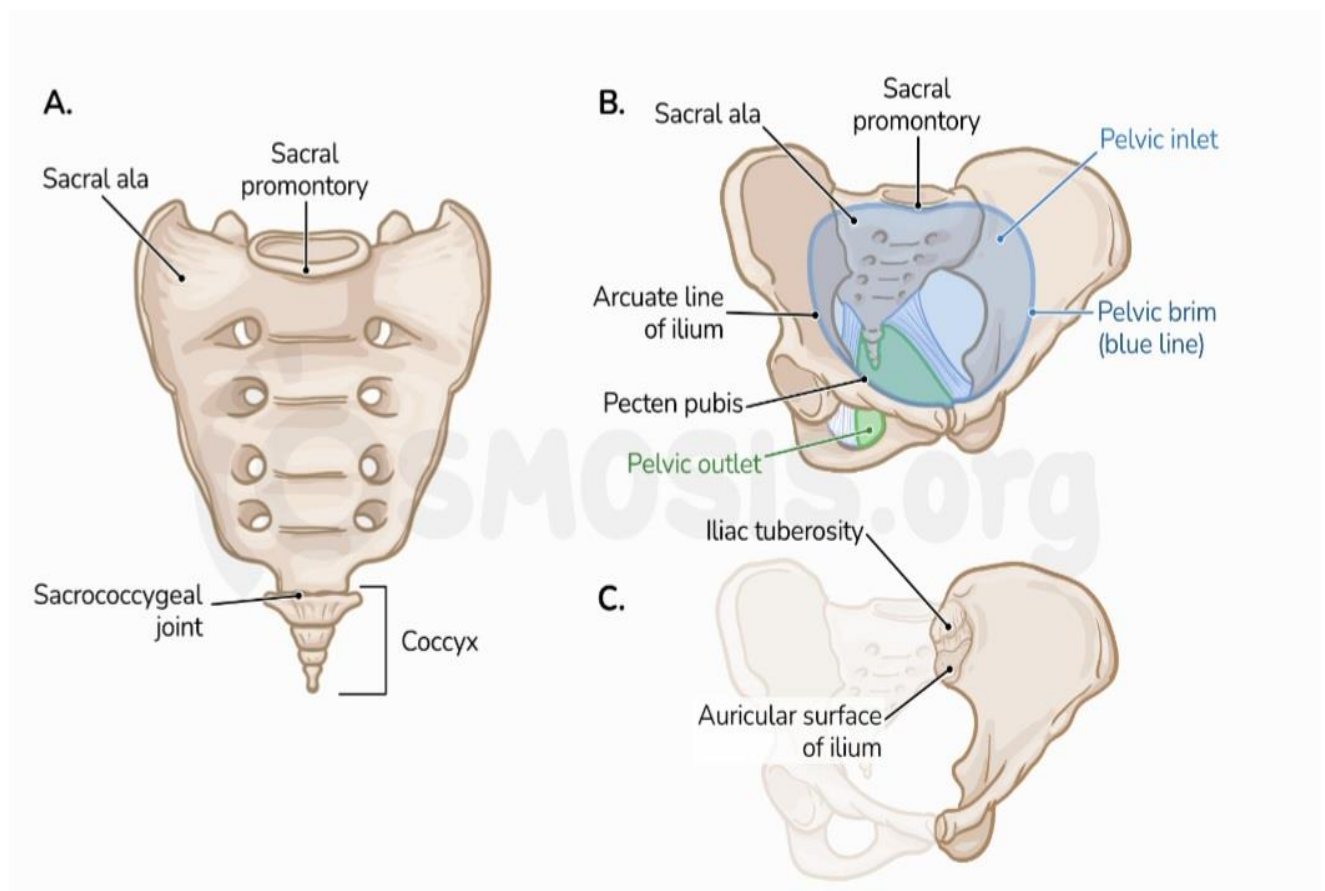
• Complete uterine prolapse /Direct support of uterus lost, Ligament involved = Lateral cervical / cardinal ligament
• Cystocele prolapsing through vaginal introitus : pubovesical and vesicocervical fascia involvement
• Moderate uterine prolapse and direct support of uterus ligament involved = Uterosacral ligament
• Dynamic support of uterus is provided by pelvic diaphragm. Cardinal ligament transmits uterine vessels .
• Labia majora contains termination of round ligament of uterus. Inguinal canal contain round ligament of uterus
• Infundibulopelvic ligament or suspensory ligament of ovary contains ovarian vessels and nerves
• Gubernaculum in female give rise to round ligament of uterus and round ligament ovaries

VAGINA & VULVA	
Features	<ul style="list-style-type: none"> Vulva is external part of genitalia including labia, clitoris, opening of vagina and urethral opening Vagina is internal part of genitalia and the canal that connects vaginal opening to the cervix Vagina is 10cm (4 inches) long Potential space except posterior fornix which is real space Shape: Wider left to right at top and Wider anterior to posterior at introitus Epithelium: Non-keratinising stratified squamous epithelium with Smooth muscle, sweat glands. No mucous glands Upper third of vagina develops from Lower part of paramesonephric ducts Lower two thirds from urogenital sinus Hymen epithelium: stratified squamous epithelium. 3 Fornices of Vagina: Anterior, lateral & posterior Labia majora is joined to back front by anterior & posterior Commissures. Round ligament of uterus ends at anterior end of each Labia minora give clitoral prepuce. Clitoris = 2 small corpora Cavernosa. Bulb of clitoris or vestibule is a spongy erectile tissue in labia minora.
Important Relations	<ul style="list-style-type: none"> Lateral to upper part: ureter Lateral to middle part: the anterior fibres of levator ani Lateral to lower part: urogenital diagram
Glands	<ul style="list-style-type: none"> Greater vestibular glands (Bartholin glands): Round (< 1cm) glands at 4 & 8 o'clock behind bulb. 2cm duct into Posterolateral vaginal orifice in superficial perineal pouch. Homologues of Cowper's glands in males. Cysts and infection is possible here Paraurethral glands (Skene glands): Mucous glands opening just inside urethra. Homologue of prostate Lesser vestibular glands: Multiple small mucous glands opening between vagina and Urethra
Support	<ul style="list-style-type: none"> levator ani (Pubo vaginalis) and perineal body
Blood supply	<ul style="list-style-type: none"> Arteries: Vaginal branch of uterine, middle rectal, inferior Vesical gives vaginal branches Veins: Pelvic floor plexus to internal iliac vein
Nerve supply	<ul style="list-style-type: none"> Sympathetic supply by pelvic plexus (vasoconstriction, smooth muscle action + stretch sensation) Somatic supply from perineal branches of pudendal, ilioinguinal nerve at anterior introitus Posterior Fornix of vagina is Not supplied by pudendal nerve but via inferior hypogastric plexus
Lymphatics	<ul style="list-style-type: none"> External/internal iliac, sacral, superficial inguinal (Below hymen)
Clinical anatomy	<ul style="list-style-type: none"> Abscess in Rectouterine pouch or pouch of Douglas can be drained via posterior fornix. Culdocentesis A procedure involving the extraction of fluid from the pouch of Douglas. It can be one diagnostic technique used in identifying pelvic inflammatory disease and Ruptured ectopic pregnancies that cause hemoperitoneum, Pouch of Douglas is often reached through the posterior fornix of vagina. The process of creating hole is called colpotomy if a scalpel incision is used to drain fluid, not by needle. Bartholin cyst: Greater vestibular glands are involved , formed on vaginal surface Nabothian cyst: mucous filled cyst formed on the surface of cervix.



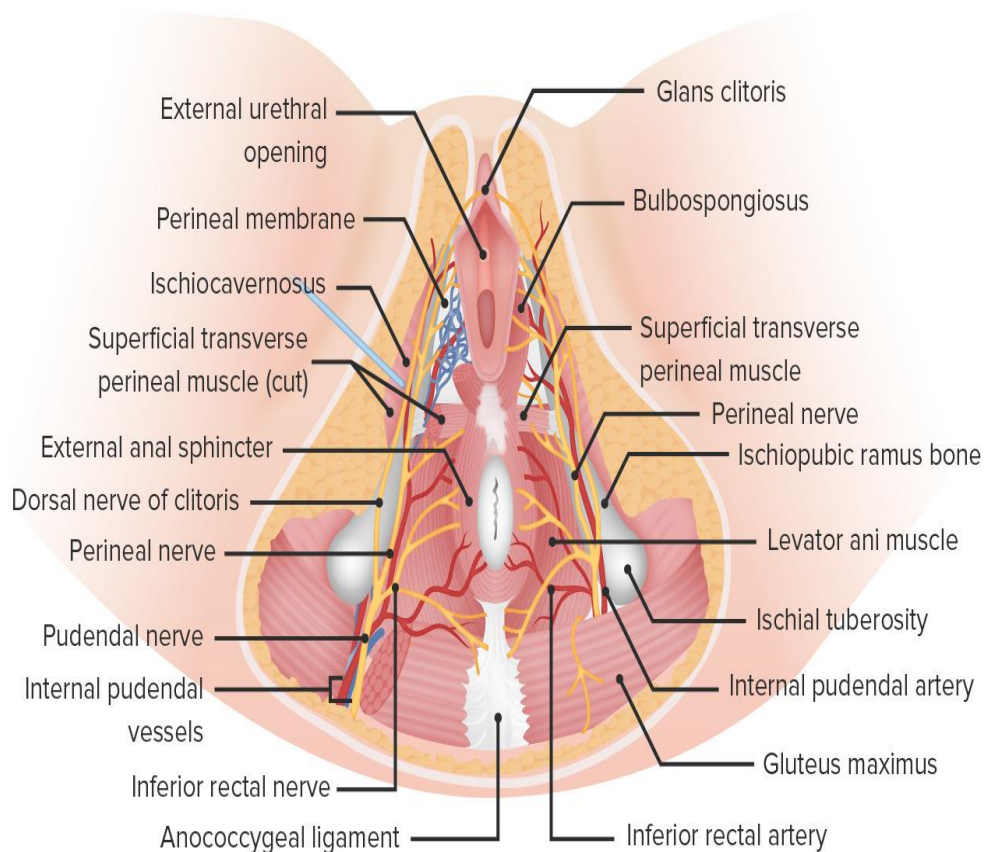
Boundaries		PELVIC INLET	PELVIC OUTLET
	Anteriorly	Symphysis pubis	Symphysis pubis
	Posteriorly	Promontory of sacrum, ala of sacrum	Coccyx
	Laterally	iliopectineal line (arcuate line)	Antero laterally: Ischiopubic ramus Posterolaterally: Sacrotuberous ligaments
TRUE PELVIS		Lies below pelvic brim, limited inferiorly by Pelvic diaphragm. It contains Colon, Rectum, Bladder, Ovaries and Uterus	
FALSE PELVIS		Lies above pelvic brim/inlet and contains abdominal organs	
MALE PELVIS		FEMALE PELVIS	
❖ Heavy rough and not wide or broad		❖ Bones are light and smooth Walls	
❖ Narrow iliac Crest		❖ Wide iliac crest	
❖ Pelvic Brim is heart shaped		❖ Brim almost round	
❖ Pelvic cavity deep and funnel shaped		❖ Cavity is shallow	
❖ Symphysis pubis is deep		❖ Symphysis pubis wide	
❖ Narrow pelvic outlet		❖ Wide transverse outlet	
❖ Subpubic angle 65-85°		❖ Sub-pubic arch is 85-90°	
❖ Sciatic notch narrow		❖ Sciatic notch wide	
❖ Ischial Spines inverted		❖ Ischial spines blunt	
Pelvis	Diameter (cm)		
	Anteroposterior	Transverse	Oblique
Pelvic inlet	11	13	12
Pelvic cavity	12	12	12
Pelvic outlet	13	11	-
AP DIAMETERS			
True conjugate (11cm)	○ Measured from sacral promontory to the centre of upper surface of the Symphysis pubis		
Obstetric conjugate (10.5 cm)	○ Extends from the sacral promontory to the upper inner border of the Symphysis pubis. ○ This is the first bony strait through Which the fetus must pass.		
Diagonal conjugate (12cm)	○ Measured Antero posteriorly from apex of pubic arch of Symphysis to sacral promontory		

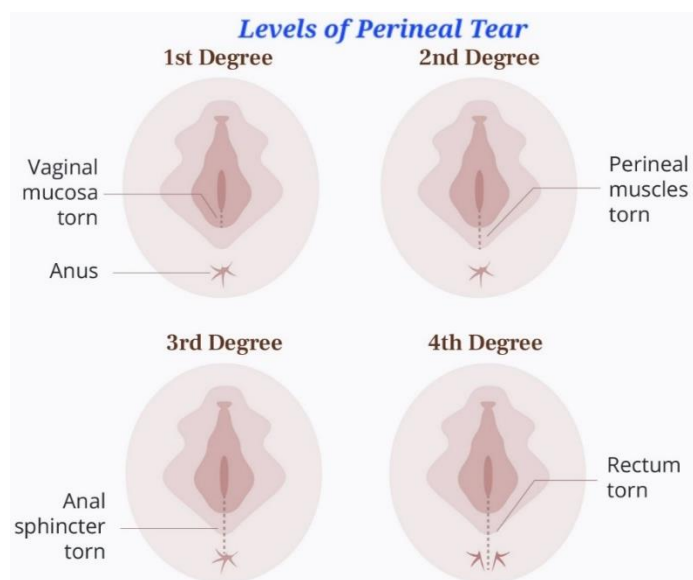
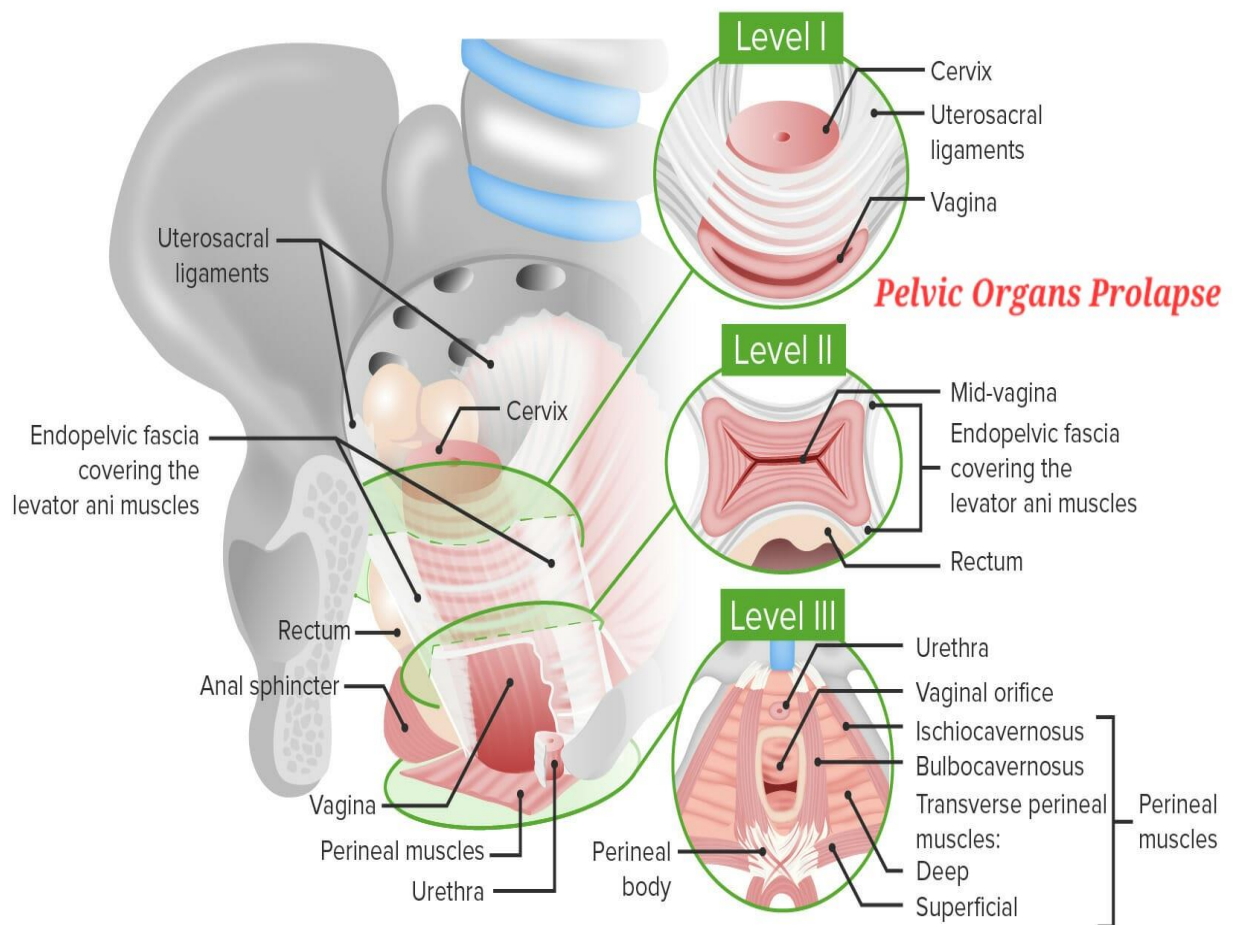
TYPES OF PELVISES ON THE BASIS OF SHAPE	
Gynaecoid pelvis	<ul style="list-style-type: none"> ❖ Typical female Pelvis, In 80% Asian females, Oval-shaped. ❖ Most suitable pelvis for vaginal delivery ❖ More transverse diameter than Anteroposterior diameter and has good sacral curve
Android pelvis	<ul style="list-style-type: none"> ❖ Typical male pattern, triangular/heart-shaped, reduced true conjugate + prominent Ischial spine leading to decreased inter-ischial diameter. Narrow subpubic angle ❖ Most troublesome pelvis Account for a larger of Proportion difficult vaginal deliveries
Anthropoid pelvis	<ul style="list-style-type: none"> ❖ Commonest variant of Gynaecoid type, Oval, AP diameter > Transverse diameter ❖ Often high angle of inclination. Rounded in shape and sidewalls are divergent. ❖ Leads to delayed Engagement of Head
Platypelloid pelvis	<ul style="list-style-type: none"> ❖ Ricketic pattern. Flattened oval. Transverse diameter much more than AP diameter ❖ Reduced true conjugate causes delay of engagement of head leading to high incidence of caesarean section and association with face presentation



Boundaries of Perineum	<ul style="list-style-type: none"> • Anterior : lower border of Symphysis pubis & arcuate Pubic ligament • Posteriorly: tip of coccyx. • Antero-laterally: Ischiopubic rami and ischial tuberosities • Postero-laterally: Sacrotuberous ligament 						
Pelvic floor muscles	<p>It consists of three muscle layers:</p> <table border="1"> <tr> <td>Superficial perineal layer</td><td> <ul style="list-style-type: none"> • innervated by the pudendal nerve. This layer consists of; • Bulbocavernosus, Ischiocavernosus, Superficial transverse perineal muscles, External anal sphincter (EAS) </td></tr> <tr> <td>Deep Urogenital diaphragm layer</td><td> <ul style="list-style-type: none"> • innervated by pudendal nerve • Compressor urethra, ureterovaginal sphincter, deep transverse perineal </td></tr> <tr> <td>Pelvic diaphragm</td><td> <ul style="list-style-type: none"> • innervated by sacral nerve roots S3-S5 • Levator Ani (pubococcygeus puborectalis, iliococcygeus) • Coccygeus/ischiococcygeus, Piriformis and Obturator internus </td></tr> </table>	Superficial perineal layer	<ul style="list-style-type: none"> • innervated by the pudendal nerve. This layer consists of; • Bulbocavernosus, Ischiocavernosus, Superficial transverse perineal muscles, External anal sphincter (EAS) 	Deep Urogenital diaphragm layer	<ul style="list-style-type: none"> • innervated by pudendal nerve • Compressor urethra, ureterovaginal sphincter, deep transverse perineal 	Pelvic diaphragm	<ul style="list-style-type: none"> • innervated by sacral nerve roots S3-S5 • Levator Ani (pubococcygeus puborectalis, iliococcygeus) • Coccygeus/ischiococcygeus, Piriformis and Obturator internus
Superficial perineal layer	<ul style="list-style-type: none"> • innervated by the pudendal nerve. This layer consists of; • Bulbocavernosus, Ischiocavernosus, Superficial transverse perineal muscles, External anal sphincter (EAS) 						
Deep Urogenital diaphragm layer	<ul style="list-style-type: none"> • innervated by pudendal nerve • Compressor urethra, ureterovaginal sphincter, deep transverse perineal 						
Pelvic diaphragm	<ul style="list-style-type: none"> • innervated by sacral nerve roots S3-S5 • Levator Ani (pubococcygeus puborectalis, iliococcygeus) • Coccygeus/ischiococcygeus, Piriformis and Obturator internus 						
Pelvic diaphragm	<ul style="list-style-type: none"> • Pelvic Diaphragm = Levator Ani + Coccygeus muscle • Muscular partition between the true pelvis and the perineum is known as the pelvic diaphragm. • A gutter-shaped pelvic floor is created by this diaphragm. It is created by the large levator ani and Small coccygeus muscles of 2 sides and their covering fasciae. • It is incomplete anteriorly to allow passage of urethra in the males and vagina in the Females. • Functions <ul style="list-style-type: none"> • Main support to the pelvic viscera and has sphincteric actions on the rectum and vagina • Dynamic support of the uterus is provided by the pelvic diaphragm • The intra-abdominal pressure during defecation, micturition, and parturition is raised with its help. • Clinical Correlations: <ul style="list-style-type: none"> • The pelvic diaphragm could be injured (tearing of perineal Body) during challenging childbirth. This may result in uterine Prolapse and Rectal Prolapse. 						
Urogenital diaphragm	<p>Urogenital diaphragm = Deep Transverse Perineal muscles + Sphincter urethra muscle</p> <ul style="list-style-type: none"> • A triangle shaped muscle layer created by sphincter urethrae along with deep transverse Perineal. They are confined among superior and inferior layer of the fascia of the urogenital diaphragm. • The inferior layer of fascia is often called as the perineal membrane. • The external urethral sphincter is present in urogenital diaphragm • Composition: <ul style="list-style-type: none"> • it has two fasciae called Inferior layer of the diaphragm or the perineal membrane • Superior layer of the diaphragm • confined space enclosed among superficial and deep layers of fascia is called deep perineal pouch • Attachment <ul style="list-style-type: none"> • Anteriorly, two layers of fascia merge, leaving behind a small space beneath the Symphysis pubis. • Posteriorly, two layers of fascia fuse with each other as well as with the membranous layer of the superficial fascia along with the perineal body. • Laterally the layers of fascia are connected to the pubic arch. 						
Urogenital triangle	<ul style="list-style-type: none"> • Urogenital triangle is the anterior half of perineum oriented in the horizontal plane • triangular in shape, composed of roots of external genitalia and openings of the urogenital system. The urogenital triangle of the perineum is defined as: • Laterally by the ischiopubic rami. • Posteriorly by an imaginary line b/w the ischial tuberosities. • Anteriorly by the inferior margin of the Pubic Symphysis. 						

	<ul style="list-style-type: none"> As with the anal triangle, roof or ceiling of the urogenital triangle is the levator ani muscle. Unlike the anal triangle, the urogenital triangle contains a strong fibromuscular support platform, the perineal membrane and deep perineal pouch, which is attached to the pubic arch. Anterior extensions of ischio-anal fossa occur between the deep perineal pouch and the levator ani muscle on each side 	
Perineal pouches	Superficial Perineal pouch <u>Contents</u> <ul style="list-style-type: none"> Structure forming root of penis/clitoris Bulbospongiosus muscle Ischiocavernosus muscle Superficial transverse perineal muscle Perineal branch of the pudendal nerve Perineal body Greater vestibular glands (Bartholin glands) 	Deep perineal pouch <u>Contents</u> <ul style="list-style-type: none"> Membranous part of the urethra Sphincter urethra muscle Deep transverse perineal muscle Internal pudendal vessels and its branches Dorsal vein of clitoris/penis Bulbourethral gland (Cowper's gland)





Rectouterine pouch	<ul style="list-style-type: none"> Also known as the rectovaginal pouch or pouch of Douglas An extension of peritoneum between posterior wall of uterus and rectum in females. It is the most dependent part of peritoneal cavity and analogous to rectovesical pouch in males
ISCHIORECTAL FOSSA	
Introduction	<p>Wedge shape space contains fat pads</p> <p>Allows movement of the pelvic diaphragm and expansion of the anal Canal during defecation</p> <p>Conveys pudendal nerve + internal pudendal vessels from lesser sciatic notch to deep perineal pouch</p>
Boundaries	<ul style="list-style-type: none"> ❖ Perineal skin forms the base ❖ Lateral wall formed by ischium, obturator internus muscle, and the sacrotuberous ligament ❖ Medial wall consists of levator ani muscle
Contents	<ul style="list-style-type: none"> ❖ Pudendal nerve and its branches, Internal pudendal vessels, Pudendal canal and its content ❖ Ischiorectal pad and fat <p>The pudendal (Alcock's) canal is a sheath in the lateral wall of the Ischiorectal fossa.</p>
PERINEAL BODY	<ul style="list-style-type: none"> ❖ A pyramidal fibromuscular mass in the middle line of perineum at the Junction between the urogenital triangle and the anal triangle. It is found in both males and Females. ❖ Located About 1.25 cm in front of the anal margin and close to the penis ❖ Function: it is important in females for the support of the pelvic organs. ❖ There is no attachment or insertion of ischiocavernosus muscle on perineal body ❖ Muscle forming perineal body: BLESSED Bulbospongiosus, Levator ani, External anal sphincter, Superficial transverse perinei, Sphincter urethra and Deep transverse perinei ❖ Perineal body can also be disrupted by trauma, inflammatory disease and infection, which may produce fistula that connected to the vestibule of the vagina. ❖ In women, it acts as a tear-resistant body between the vagina and the external anal Sphincter, supporting the posterior part of the vaginal wall against Prolapse. ❖ In males ,It lies between the bulb of the penis and the anus. ❖ Childbirth can lead to damage (stretching/tearing) of the perineal body, thus leading to Possible Prolapse of pelvic viscera
Ischial Spine	<ul style="list-style-type: none"> ❖ It is the bony landmark during childbirth, for pudendal anaesthesia (stage-1I) ❖ It is a landmark for Bishop scoring. Inverted Ischial spine is seen in the anthropoid pelvis ❖ Ureter enter bladder at the Ischial spine
Episiotomy (Median or mediolateral)	<ul style="list-style-type: none"> ❖ Episiotomy is a planned incision made in the perineum in posterolateral Direction by cutting the tissue between the vaginal opening and the anus during Childbirth. This is done to enlarge the vaginal opening to facilitate the childbirth thereby preventing the tear of the perineal body. ❖ The main disadvantage of midline episiotomy is the risk of the external anal sphincter injury ❖ Muscles which are cut in Midline Episiotomy are: Bulbospongiosus muscle and Superficial transverse perineal muscle
Blood + Nerve supply of Perineum	
<p>Internal pudendal artery → inferior rectal, perineal, and dorsal artery of clitoris.</p> <p>Pudendal nerve → inferior rectal, perineal, and dorsal nerve of clitoris.</p>	

INGUINAL CANAL	
Boundaries	<ul style="list-style-type: none"> ❖ MALT = Muscles, Aponeurosis, Ligament and Tendon + Transversalis fascia ❖ Superior wall (roof) 2 Muscles (Internal oblique Muscle and transverse abdominis Muscle) ❖ Anterior wall: 2 Aponeurosis (Aponeurosis of internal oblique and external oblique) ❖ Lower wall (Floor): 2 ligaments : inguinal Ligament and lacunar Ligament ❖ Posterior wall 2Ts : Transversalis fascia and Conjoined Tendon
Contents	<ul style="list-style-type: none"> ❖ Structures passing through canal: <ul style="list-style-type: none"> ✓ Spermatic cord in male and round ligament of uterus in female ✓ Ilioinguinal nerve
Spermatic cord	<ul style="list-style-type: none"> ❖ Structures and Contents: 3 fascia + 3 arteries + 3 veins + 2 nerves ❖ Fascia: external spermatic fascia, cremasteric fascia, internal spermatic fascia ❖ Artery: testicular artery, cremasteric artery. deferential Artery ❖ Vein: pampiniform plexus & testicular vein, cremasteric vein ❖ Nerve: Genital branch of genitofemoral (L2), Sympathetic plexus

Inguinal Hernia	Direct Inguinal hernia		Indirect Inguinal hernia	
	Pathology: <ul style="list-style-type: none"> • Chronic increased intraabdominal pressure • Advanced age in males • Weakness of transversalis fascia • Herniates through the Hesselbach triangle Boundaries: <ul style="list-style-type: none"> • Medially: lateral border of rectus abdominis • Laterally: inferior epigastric artery • Inferiorly: Inguinal ligament (hernia is medial) Clinical Features: May precipitate intestinal obstruction: Abdominal pain, Nausea, Vomiting, Distention		Pathology: Seen in Male infants + young adults. Patent processus vaginalis Protrudes through the deep inguinal ring into the inguinal canal. May extend into the scrotum.	
Femoral Hernia			Boundaries: Medially: inferior epigastric artery Inferiorly: inguinal ligament	
			Clinical Features: <ul style="list-style-type: none"> • Asymptomatic, Visible bulge • Reducible mostly • Hernia is lateral to inferior epigastric artery 	
	It occurs in Advanced age females due to Laxity of femoral ring. Herniates through the femoral ring into the femoral canal Femoral hernia lies inferomedially to pubic tubercle			
		Boundaries	Clinical features	
		Superolaterally: inguinal ligament Medially: pubic tubercle Laterally: femoral vein Inferioposteriorly: iliopectineal ligament	<ul style="list-style-type: none"> • Incarceration and/or strangulation of the herniated bowel • Abdominal pain • Nausea, Vomiting • abdominal distention 	

ABDOMINAL AORTA (T12 – L4)

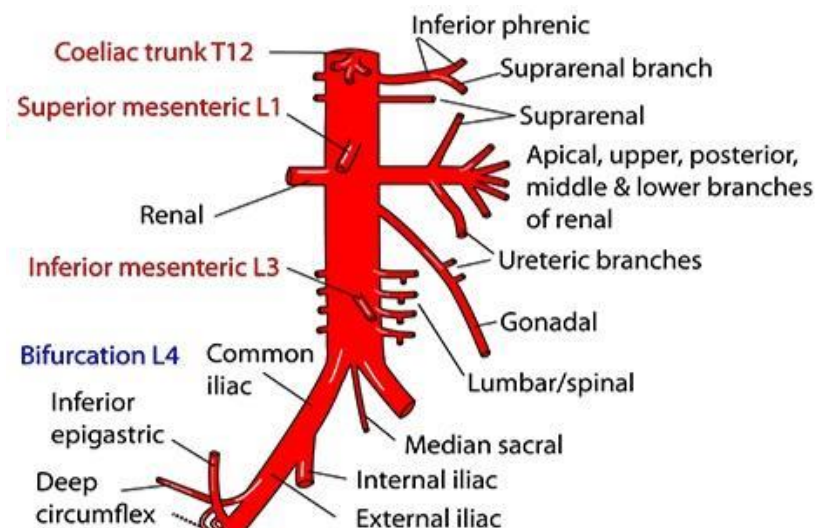
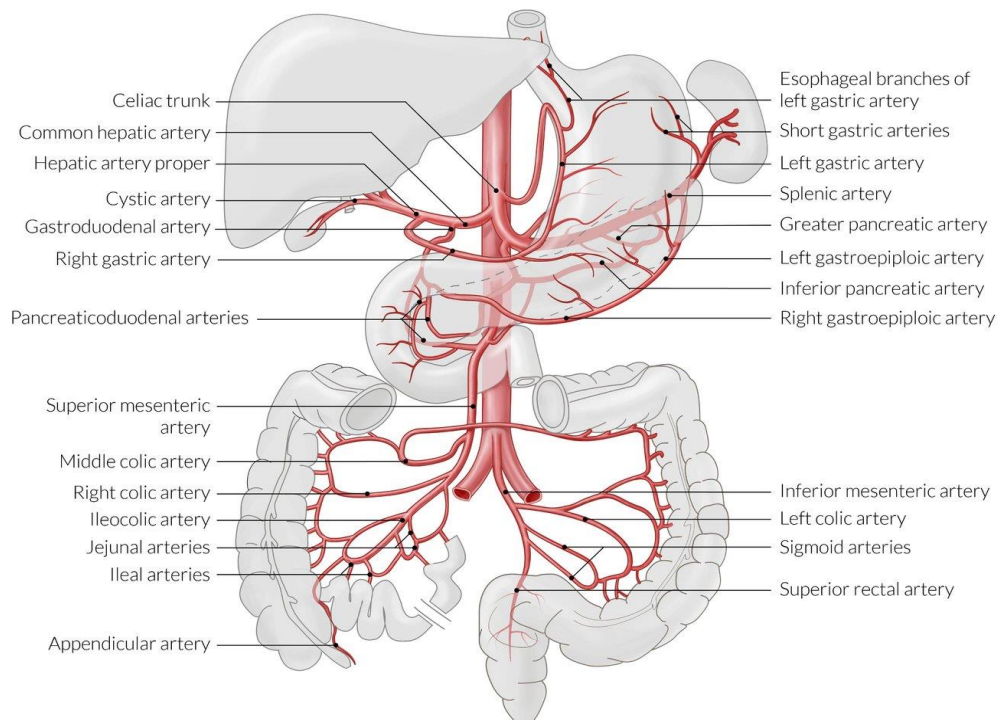
ABDOMINAL AORTA (T12 – L4)								
Relations	<ul style="list-style-type: none">On its right side lies inferior vena cava, the cisterna chyli, and the beginning of the Azygos Vein.On its left side lies the left sympathetic trunk.Anterior: Pancreas, splenic vein, left renal vein, third part duodenum, mesentery, nodes, autonomic plexus, lesser sac, stomach, omentum, small bowelPosterior: T12-L4 vertebrae, left lumbar veinsAorta is largest artery in body, begins at T12, ends at L4 with bifurcation into the common iliacThe summit of its convexity corresponds to the third lumbar vertebra.							
Branches	<ul style="list-style-type: none">Inferior phrenic arteries: first branches Abd aorta originating just above the celiac trunk.Three anterior visceral branches (Single): The celiac artery, superior mesenteric artery, and Inferior mesenteric arteryThree lateral visceral branches (Paired): The suprarenal artery, renal artery, and testicular or Ovarian arteryFive lateral abdominal wall branches (Paired): The inferior phrenic artery and four lumbar ArteriesThree terminal branches: The two common iliac arteries and the median sacral artery							
Celiac Trunk (T12)	<p>Branches- Mnemonics (LHS) = Left Gastric artery, Common Hepatic artery, Splenic Artery.</p> <table><tr><td>Left gastric</td><td>Supplies the lower third of the esophagus and upper right of the Stomach. It is the smallest branch</td></tr><tr><td>Common Hepatic artery</td><td><p>Branches = Right gastric, Gastroduodenal artery, Terminal branches (Hepatic arteries)</p><ul style="list-style-type: none">Right gastric artery supplies lower right part of the stomach + First 2cm of duodenum or duodenal cap.Gastroduodenal artery - branches of Gastroduodenal artery :<ul style="list-style-type: none">Right gastroepiploic artery: Supplies the stomach along lower Greater curvature.Superior pancreaticoduodenal arteryTerminal branches<ul style="list-style-type: none">Right hepatic artery gives cystic artery which supplies gallbladder and CBDLeft hepatic artery<p>Variations:</p><ul style="list-style-type: none">☆ Replaced / Accessory right hepatic artery- arises from SMA (20%)♂ Replaced/ Accessory left hepatic artery- arises from left gastric artery (15%)</td></tr><tr><td>Splenic artery</td><td><p>Largest branch of celiac trunk .Its branches supply the body and tail of pancreas.</p><p>Branches: Short gastric artery, Left gastroepiploic artery, Greater pancreatic artery</p><ul style="list-style-type: none">Short gastric artery: Supplies the fundus. Short gastric artery has poor Anastomosis and would be affected by pressure on splenic arteryLeft gastroepiploic artery: Supply the stomach along upper greater CurvatureGreater pancreatic artery (arteria pancreatica magna) is the Largest artery that supplies the pancreas. It arises from the splenic artery.Small branch, which runs toward tail, is referred to as arteria caudae pancreatica.</td></tr></table>		Left gastric	Supplies the lower third of the esophagus and upper right of the Stomach. It is the smallest branch	Common Hepatic artery	<p>Branches = Right gastric, Gastroduodenal artery, Terminal branches (Hepatic arteries)</p> <ul style="list-style-type: none">Right gastric artery supplies lower right part of the stomach + First 2cm of duodenum or duodenal cap.Gastroduodenal artery - branches of Gastroduodenal artery :<ul style="list-style-type: none">Right gastroepiploic artery: Supplies the stomach along lower Greater curvature.Superior pancreaticoduodenal arteryTerminal branches<ul style="list-style-type: none">Right hepatic artery gives cystic artery which supplies gallbladder and CBDLeft hepatic artery <p>Variations:</p> <ul style="list-style-type: none">☆ Replaced / Accessory right hepatic artery- arises from SMA (20%)♂ Replaced/ Accessory left hepatic artery- arises from left gastric artery (15%)	Splenic artery	<p>Largest branch of celiac trunk .Its branches supply the body and tail of pancreas.</p> <p>Branches: Short gastric artery, Left gastroepiploic artery, Greater pancreatic artery</p> <ul style="list-style-type: none">Short gastric artery: Supplies the fundus. Short gastric artery has poor Anastomosis and would be affected by pressure on splenic arteryLeft gastroepiploic artery: Supply the stomach along upper greater CurvatureGreater pancreatic artery (arteria pancreatica magna) is the Largest artery that supplies the pancreas. It arises from the splenic artery.Small branch, which runs toward tail, is referred to as arteria caudae pancreatica.
Left gastric	Supplies the lower third of the esophagus and upper right of the Stomach. It is the smallest branch							
Common Hepatic artery	<p>Branches = Right gastric, Gastroduodenal artery, Terminal branches (Hepatic arteries)</p> <ul style="list-style-type: none">Right gastric artery supplies lower right part of the stomach + First 2cm of duodenum or duodenal cap.Gastroduodenal artery - branches of Gastroduodenal artery :<ul style="list-style-type: none">Right gastroepiploic artery: Supplies the stomach along lower Greater curvature.Superior pancreaticoduodenal arteryTerminal branches<ul style="list-style-type: none">Right hepatic artery gives cystic artery which supplies gallbladder and CBDLeft hepatic artery <p>Variations:</p> <ul style="list-style-type: none">☆ Replaced / Accessory right hepatic artery- arises from SMA (20%)♂ Replaced/ Accessory left hepatic artery- arises from left gastric artery (15%)							
Splenic artery	<p>Largest branch of celiac trunk .Its branches supply the body and tail of pancreas.</p> <p>Branches: Short gastric artery, Left gastroepiploic artery, Greater pancreatic artery</p> <ul style="list-style-type: none">Short gastric artery: Supplies the fundus. Short gastric artery has poor Anastomosis and would be affected by pressure on splenic arteryLeft gastroepiploic artery: Supply the stomach along upper greater CurvatureGreater pancreatic artery (arteria pancreatica magna) is the Largest artery that supplies the pancreas. It arises from the splenic artery.Small branch, which runs toward tail, is referred to as arteria caudae pancreatica.							
Superior mesenteric artery (SMA) (L1)	<ul style="list-style-type: none">Abdominal angina occurs due to obstruction of SMASuperior and inferior mesenteric artery are joined by marginal artery at 2/3rd of Transverse colonSuperior and inferior mesenteric artery overlap at splenic flexure (watershed Area)SMA is crossed anteriorly by the splenic vein and the neck of pancreas, posterior to the SMA are the left renal vein, the uncinate process and the third part of duodenum.Branches<table><tr><td>Inferior pancreaticodudenal</td><td>1st branch, Supplies head of pancreas, ascending + inferior duodenum</td></tr><tr><td>Jejunal and ileal</td><td>Supply jejunum and ileum</td></tr><tr><td>ileocolic artery</td><td>Jejunal and ileal passes downward and to the right towards the right iliac fossa where it divides into superior and inferior branches: The superior branch passes upward along the ascending colon to anastomoses with the right colic artery;</td></tr></table>		Inferior pancreaticodudenal	1st branch, Supplies head of pancreas, ascending + inferior duodenum	Jejunal and ileal	Supply jejunum and ileum	ileocolic artery	Jejunal and ileal passes downward and to the right towards the right iliac fossa where it divides into superior and inferior branches: The superior branch passes upward along the ascending colon to anastomoses with the right colic artery;
Inferior pancreaticodudenal	1st branch, Supplies head of pancreas, ascending + inferior duodenum							
Jejunal and ileal	Supply jejunum and ileum							
ileocolic artery	Jejunal and ileal passes downward and to the right towards the right iliac fossa where it divides into superior and inferior branches: The superior branch passes upward along the ascending colon to anastomoses with the right colic artery;							

		The inferior branch dividing into colic, Caecal, appendicular, ileal branches							
	Right colic artery	Supplying the ascending colon. It divides into two terminal branches – an ascending branch and a descending branch which form anastomoses with the middle colic artery, and ileocolic artery (respectively).							
	Middle colic artery	Up to right 2/3 rd of transverse colon							
Inferior mesenteric artery (IMA) (L3)	<p>Smallest branch of coeliac trunk ; gives following branches :</p> <ul style="list-style-type: none">• Left colic artery supplies left 1/3rd of transverse colon• Sigmoidal artery—2 or 3 in number• Superior rectal artery is continuation of IMA and Supplies rectum plus upper 1/3” of anal canal.• The ascent of horseshoe shaped kidney is prevented by inferior mesenteric artery								
Renal artery (L2)	<ul style="list-style-type: none">• Arise directly from aorta at L2. Right renal artery is normally longer than the left renal artery• Systolic BP is highest in renal artery. The origin of renal arteries is landmark in the abdominal aortic aneurysm surgery.• Aortic aneurysm happens below origin of the Renal arteries (95%)								
Gonadal vessels (Ovarian + Testicular)	<ul style="list-style-type: none">• Arise directly from aorta at level of L2• On each side, the vessels travel in the suspensory ligament of ovary (infundibulopelvic Ligament) as they cross the pelvic inlet to the ovary• Right ovarian/testicular artery arise from aorta, and aorta is on left side so right Ovarian/testicular artery will pass in front /anterior to IVC to lie on the right side of IVC• Branches pass through mesovarium to reach the ovary and through the broad ligament to anastomose with the uterine artery.• The ovarian arteries enlarge significantly during pregnancy to augment uterine blood supply and it Damage during hysterectomy at the level of pelvic brim								
Terminal branches	<ul style="list-style-type: none">• Common iliac Arteries & Median Sacral Artery <u>Common iliac Arteries</u> The Right and left common iliac arteries are the terminal branches of the aorta. They arise at the level of L4 and run downward and laterally along Medial border of the psoas Each artery ends in front of the sacroiliac joint by dividing into the external & internal iliac At the bifurcation, the common iliac artery on each side is crossed anteriorly by the ureter <table><tr><td>External Iliac artery</td><td><u>Branches</u><ul style="list-style-type: none">• <u>Inferior epigastric artery</u> moves upwards around the medial side of the deep Inguinal ring, enters the rectus sheath and is a landmark to differentiate b/w direct and indirect inguinal hernia. lateral end of Hesselbach’s inguinal triangle is formed by inferior epigastric artery Commonly injured in suprapubic incision Branches of Inf Epigastric artery are Accessory obturator artery & cremasteric artery• <u>Deep circumflex iliac artery</u></td></tr><tr><td>Internal iliac artery</td><td><table><tr><td><u>Branches of Anterior division</u></td><td>Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent</td></tr></table></td></tr></table>			External Iliac artery	<u>Branches</u> <ul style="list-style-type: none">• <u>Inferior epigastric artery</u> moves upwards around the medial side of the deep Inguinal ring, enters the rectus sheath and is a landmark to differentiate b/w direct and indirect inguinal hernia. lateral end of Hesselbach’s inguinal triangle is formed by inferior epigastric artery Commonly injured in suprapubic incision Branches of Inf Epigastric artery are Accessory obturator artery & cremasteric artery• <u>Deep circumflex iliac artery</u>	Internal iliac artery	<table><tr><td><u>Branches of Anterior division</u></td><td>Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent</td></tr></table>	<u>Branches of Anterior division</u>	Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent
External Iliac artery	<u>Branches</u> <ul style="list-style-type: none">• <u>Inferior epigastric artery</u> moves upwards around the medial side of the deep Inguinal ring, enters the rectus sheath and is a landmark to differentiate b/w direct and indirect inguinal hernia. lateral end of Hesselbach’s inguinal triangle is formed by inferior epigastric artery Commonly injured in suprapubic incision Branches of Inf Epigastric artery are Accessory obturator artery & cremasteric artery• <u>Deep circumflex iliac artery</u>								
Internal iliac artery	<table><tr><td><u>Branches of Anterior division</u></td><td>Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent</td></tr></table>	<u>Branches of Anterior division</u>	Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent						
<u>Branches of Anterior division</u>	Umbilical artery is the first branch of anterior trunk Branch of umbilical artery is Superior vesical artery Uterine artery: Pass in front of ureter to supply uterus. Commonly injured during C-section Vaginal artery, Obturator artery, Inferior vesical artery, Inferior Gluteal artery, Internal pudendal artery, Inferior rectal Middle rectal artery: Remains in true pelvis and cross from medial to lateral side of pelvis, may be congenitally absent								

			The middle rectal arteries are unimportant because they supply only the Superficial layers of the rectum
		Branches of Posterior division	<ul style="list-style-type: none">• Superior Gluteal artery: The largest branch of the internal iliac artery and is the terminal continuation of the posterior trunk• iliolumbar artery and Lateral sacral artery

Internal iliac artery can be injured during the removal of ovaries (oophorectomy) or Ovarian mass from ovarian fossa

- **Median Sacral Artery (Unpaired branch)**
originates from posterior surface of aorta superior to aortic bifurcation at L4 in the abdomen.



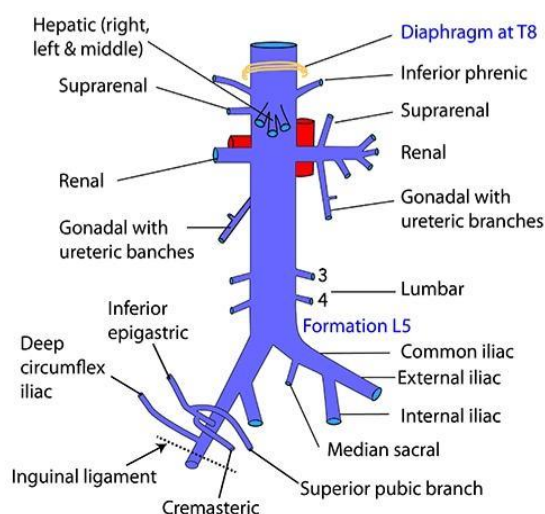
PORTAL VEIN (L2)											
Formation	<p>Formed by the Union of SMV + Splenic vein behind the neck of pancreas at the level of L2.</p> <p>Arrangement of structures in lesser omentum from anterior to posterior = DAV Bile Duct, Hepatic Artery and Portal Vein (posterior)</p>										
Parts	Supra duodenal, Retro duodenal and infra duodenal										
Tributaries	<ul style="list-style-type: none"> • Superior mesenteric vein Tributaries of SMV are the Veins corresponding to the branches of SMA They include = Inferior pancreaticoduodenal vein and right gastroepiploic vein • Splenic vein tributaries of splenic vein—Veins corresponding to the branches of splenic Artery and IMV • Right and left gastric vein • Cystic vein • Superior pancreaticoduodenal vein • Paraumbilical vein 										
Porto-Caval OR Portosystemic anastomosis	<div data-bbox="667 757 1276 1370" data-label="Image"> </div> <p>Anastomoses that occur between the veins of the portal circulation & of the systemic Circulation</p> <table border="1"> <thead> <tr> <th>SITE</th><th>ANASTOMOSIS + CLINICAL SIGNIFICANCE</th></tr> </thead> <tbody> <tr> <td>Esophagus</td><td> <ul style="list-style-type: none"> ○ B/w Left gastric vein (Portal) and esophageal vein (systemic) ○ In Esophageal varices left gastric vein is involved. </td></tr> <tr> <td>Umbilicus</td><td> <ul style="list-style-type: none"> ○ Paraumbilical vein (portal) and Anterior abdominal vein (systemic)- ○ Caput medusae appearance due to paraumbilical veins involvement </td></tr> <tr> <td>Rectum</td><td> <ul style="list-style-type: none"> ○ Superior rectal vein (portal) , middle and inferior rectal vein (systemic) ○ Internal haemorrhoids result due to SRV involvement </td></tr> <tr> <td>Bare Area of Liver</td><td> <ul style="list-style-type: none"> ○ b/w branch of Portal vein and hepatic veins </td></tr> </tbody> </table>	SITE	ANASTOMOSIS + CLINICAL SIGNIFICANCE	Esophagus	<ul style="list-style-type: none"> ○ B/w Left gastric vein (Portal) and esophageal vein (systemic) ○ In Esophageal varices left gastric vein is involved. 	Umbilicus	<ul style="list-style-type: none"> ○ Paraumbilical vein (portal) and Anterior abdominal vein (systemic)- ○ Caput medusae appearance due to paraumbilical veins involvement 	Rectum	<ul style="list-style-type: none"> ○ Superior rectal vein (portal) , middle and inferior rectal vein (systemic) ○ Internal haemorrhoids result due to SRV involvement 	Bare Area of Liver	<ul style="list-style-type: none"> ○ b/w branch of Portal vein and hepatic veins
SITE	ANASTOMOSIS + CLINICAL SIGNIFICANCE										
Esophagus	<ul style="list-style-type: none"> ○ B/w Left gastric vein (Portal) and esophageal vein (systemic) ○ In Esophageal varices left gastric vein is involved. 										
Umbilicus	<ul style="list-style-type: none"> ○ Paraumbilical vein (portal) and Anterior abdominal vein (systemic)- ○ Caput medusae appearance due to paraumbilical veins involvement 										
Rectum	<ul style="list-style-type: none"> ○ Superior rectal vein (portal) , middle and inferior rectal vein (systemic) ○ Internal haemorrhoids result due to SRV involvement 										
Bare Area of Liver	<ul style="list-style-type: none"> ○ b/w branch of Portal vein and hepatic veins 										

KEY FACTS – RECTAL VEINS

- **Superior rectal vein** continues upward as IMV, open into the splenic vein Which joins the SMV to form portal vein.
- The haemorrhoids are varicosities of the tributaries of SRV and are covered by mucous membrane.
- The superior rectal vein is the most dependent part of the portal circulation and is Valveless
- **Inferior rectal vein** drains into the internal pudendal vein, which drains into internal iliac vein
- **Internal iliac vein** joins the external iliac vein to form the common Iliac vein, thus, forming IVC
- **Middle rectal vein** drains into the anterior division of internal iliac vein

INFERIOR VENA CAVA (L5 – T8)

Formation	<ul style="list-style-type: none"> • IVC is the largest vein in the human body, great saphenous vein is the longest vein in the body. • Formed by Union of Rt and Lt Common iliac veins at right side of midline • passes through vena caval opening of diaphragm at T8 and goes from L5-T8 (Remember; digit 58)
Tributaries	<p>Mnemonics = I Like To Rise So High Common iliac, Lumbar, Testicular(Right), Renal, Suprarenal, Hepatic veins</p> <ul style="list-style-type: none"> • Right renal vein, right suprarenal vein and right testicular/ovarian vein drain directly into IVC • Left suprarenal/adrenal vein and left testicular/ovarian first drain into left renal vein and then left renal vein open directly into IVC • Inferior phrenic vein and four lumbar veins • Two common iliac vein (external iliac and internal iliac vein) and median sacral vein • Two Hepatic veins • Note: NO tributaries from gut <p>Right sided veins (Testicular/Ovarian and Suprarenal veins) drain directly into IVC because IVC Is on right side while left sided veins (Testicular/Ovarian and Suprarenal veins) first drain into left renal vein which Passes in front of aorta to drain into IVC</p> <p>The longer left renal vein crosses the midline anterior to the abdominal aorta and posterior to the superior mesenteric artery and can be compressed by an aneurysm in Either of these two vessels</p>
Relations	<ul style="list-style-type: none"> • Anterior: Bile duct, liver, opening of lesser sac, 1st /3rd parts of duodenum, head of pancreas, small bowel, right Common iliac artery, root of mesentery, right Gonadal artery, portal vein • Posterior: Right renal artery, lumbar arteries, right crus of Diaphragm, right suprarenal & its artery, bodies of L3,4,5 vertebrae, right psoas, right sympathetic chain, right coeliac ganglion
Clinical anatomy	<ul style="list-style-type: none"> • IVC is primarily a right-sided structure, unconscious pregnant women should be Turned on to their left side (the recovery position), to relieve pressure on it and facilitate Venous return • Any surgical procedure involving the thoracic cavity or abdomen Requires attention to the location, condition, and orientation of the inferior vena cava in Relation to other structures and organs. Injury to the IVC can result in significant blood loss if Not corrected promptly.



REFERRED PAIN FROM VISCERA	SITE / SEGMENT INVOLVED
Gall bladder & shoulder Pain referred from Pleura	For both conditions : Phrenic nerve- C3, C4 , C5
Epigastrium (Stomach), Small intestine	Greater splanchnic nerve ;T5—T9
Jejunum	Greater & Lesser Splanchnic Nerves
Umbilicus or Appendix	Lesser Splanchnic nerves (T10,T11) T10 via sympathetic nerves for Umbilicus, T10 - Appendix
Ovarian pain	Obturator nerve - goes to medial side of thigh
Ureteric pain to loin/ groin	Ilioinguinal nerve
Ureteric pain to Thighs & testes	Genitofemoral nerve
Intermittent pain of small intestine	Felt at Umbilicus
Pain on defecation	Pudendal nerve - S2,S3,S4
Pain in posterior thigh in Rectum carcinoma	Sacral Nerves involved
Biliary Colic	Right Hypochondrium/ Epigastric pain , T7 -T9 involvement
Angina pectoris	T1—T5 ; Thoracic splanchnic nerves
Kidneys	T11—T12
Greater splanchnic nerve root value	T5 - T9
Lesser Splanchnic nerve	T9 - T11/T12
Least splanchnic nerve	T 12
Nipple, Xiphoid, pubis	T4 (nipple), T7 (xiphoid), Pubis (T12)

Erection	Emission	Ejaculation	Female Sexual stimulation
Parasympathetic action	Sympathetic action	Pudendal nerve (Visceral + somatic)	Parasympathetic function
Pudendal Nerve (S2,S3,S4)	<ul style="list-style-type: none"> The Pudendal Nerve (S234) and the Internal Pudendal Artery are the Major Nerve and Artery Of Perineum. Pudendal Nerve also Supply the Birth Canal. But Keep in Mind for Birth Canal Hypogastric Nerve > Pudendal Nerve Motor Supply: Skeletal Muscles in The Perineum Including the External Urethral Anal Sphincters And Levator Ani (Overlaps In Supply Of The Levator Ani And External Sphincter With Branches Directly From Ventral Division Of S4) Sensory(Cutaneous) Supply: Most of The Skin of The Perineum. 		
Iliohypogastric nerve	<ul style="list-style-type: none"> Main branch of L1, Sensory and motor Pierces internal oblique above anterior superior iliac spine Pierces external oblique above superficial inguinal ring Supplies Upper buttock (lateral cutaneous branch) Transversus abdominus & internal oblique (lowest fibres) + Skin of mons pubis 		
Ilioinguinal nerve	<ul style="list-style-type: none"> Muscular collateral branch of L1, Motor and sensory Pierces internal oblique above anterior superior iliac spine Supplies: Transversus & internal oblique (lowest fibres) Conjoint tendon Then enters inguinal canal from above/lateral and leaves Via superficial inguinal ring. Supplies Upper medial thigh, anterior 1/3 scrotum, labia Majora and root of penis 		

LENGTH	STRUCTURES
4cm	Cystic duct (3-4cm),Common hepatic duct, Inguinal canal, Female urethra
5cm	Parotid duct, Submandibular duct, Left bronchi, Duodenum 1 st part, Seminal vesical (coiled)
7.5cm	Uterus, Spermatic cord, Bile duct
10cm approx.	Duodenum 3 rd part, Uterine/fallopian tube, Abdominal aorta (10-11 cm), Trachea (10-11cm), Gall bladder (7-10cm)
12cm	Rectum, Pancreas (12-15cm),Spleen, Pharynx (12-14cm)
25cm	Esophagus, Stomach, Duodenum whole, Descending colon, Ureter
45cm	Spinal Cord, Vas deferens /ductus deference, Femur, Thoracic duct

Cloacal membrane	<ul style="list-style-type: none"> ○ Membrane that covers the embryonic cloaca during the Development of the urinary and reproductive organs. ○ Formed by ectoderm and Endoderm encountering each other.
Urorectal septum	<ul style="list-style-type: none"> ○ Mesodermal septum divides cloaca into primitive urogenital sinus anteriorly and anorectal canal posteriorly. ○ Urorectal septum Separate rectum and urogenital sinus ○ Maldevelopment of Urorectal septum result in recto-vaginal fistula
Meckel's diverticulum	<ul style="list-style-type: none"> ○ Said to be present in 2% of people, 2- inches long and 2 feet from the ileocecal valve, but these statements are only 70% true. ○ May contain gastric, pancreatic, liver, carcinoid, or lymph tissue. ○ Gastric mucosa bleeds commonly ○ May attach to umbilicus via a vitello-intestinal tract which May or may not leak but may cause intestinal obstruction as A volvulus can wrap around it. Symptoms very similar to appendicitis ○ This diverticulum is a true diverticulum -- lies on ante mesenteric border of ileum

Defecation

- It is the Rectoanal reflex in adults , while in children it is the gastrocolic reflex.
- Overall, most important, or main component is the Rectoanal > anorectal reflex.
- Initiated by Mass movements.
- Mainly due to parasympathetic or carried out by parasympathetic system.
- Pain during defecation or constipation is by inferior rectal nerve > pudendal nerve.
- Pain in rectum due to rectal cancer is by involvement of the sacral nerves.

SUMMARY & PAST PAPERS BCQS

1. Peptic ulcer pain carried by Greater splanchnic nerve (fibres synapse in Celiac Ganglion)
2. Pain of Peritoneal irritation due to Peptic ulcer is carried by Intercostal Nerves
3. Umbilical artery carries deoxygenated blood to the Placenta
4. Capsule of kidney prevents -- spread of infection to opposite side
5. Structure seen looping around and going towards target organ = Rt Hepatic Artery
6. Transverse colon attached to post Abd wall via Transverse Mesocolon
7. Foul smelling stool , bloating + abdominal cramps = Stool D/R must be done
8. Thick loop with less mesentery fat & long vasa recta → Jejunum
9. Terminal part of CBD is = embedded in pancreas or lies posterior to it
10. Infarction of SMA spares = Descending Colon. Inferior epigastric is injured during Supra pubic catheterization
11. Part of Gut removed which causes fluid loss : ileum, removal of jejunum causes no fluid loss
12. Max fluid loss occurs from = COLON. Stab wound lateral to Linea alba will injure IVC
13. Small intestine pain felt at Umbilicus. Superior Rectal or IMA is a major blood supply to Rectum
14. After RTA fracture of 11 th , 12 th ribs left sided + hypotension = splenic rupture
15. IMA traps horseshoe kidney. Paradeodenal fossa contains : IMV
16. Right testicular artery is anterior to IVC while Rt renal artery is posteriorly to IVC
17. Celiac Plexus lie anterior to Aorta. Celiac Trunk is the largest Unpaired vessel of aorta
18. Pancreatic magna arises from Splenic artery. IVC starts at L5 + lies anterior to Rt adrenal gland
19. T7-T12 nerves supply Rectus abdominus ; T7-T12+ ilioinguinal +iliohypogastric nerve → Transverse abdominus
20. Renal artery enters hilum at L1/L2. Celiac plexus lies at L1. Gastro esophageal junction : T11
21. Left suprarenal vein drains into Left Renal Vein. Minor calyx receive urine from Papillae
22. Superficial fascia = Loose areolar + adipose tissue. Hepatic acinus is functional unit of Liver
23. On sigmoidoscopy, upper sigmoid colon has ulcer + previous appendectomy scar. Cause is Diverticulosis
24. Pancreas lies b/w Celiac plexus and SMA
25. Iron + Ca absorption in duodenum. Max water + electrolytes absorption in jejunum. Passive water absorption in jejunum.
26. Long chain FA absorption in Jejunum while Colon absorbs short chain FA
27. Vit B12 & Bile salts absorption in Terminal ileum. Active water absorption via aldosterone seen in Colon
28. No submucosa seen in gallbladder. T7-T9 is dermatome for Cholecystitis
29. Hepatic veins drain into IVC. Glands in submucosa of duodenum = Brunner glands
30. Jejunum contains Valvulae conniventes. Celiac nodes is the main lymph drainage of stomach
31. Vein dilated in porta HTN = Lt Gastric > Lt Colic > Rt colic
32. Median sacral artery is posterior midline branch at aortic bifurcation
33. Intestine doesn't get back in = Omphalocele
34. Gastric cancer involving left upper stomach will first drain into Pancreatic Splenic Nodes
35. Lumbar arteries arise from Aorta. Iliolumbar artery is branch of Int iliac artery
36. Lesser and greater sacs meet at Epiploic foramen. Left gastric vein drains into Portal vein
37. Appendicular artery is branch of Ileocolic artery > Posterior Caecal artery
38. Structure visible at T12 behind stomach = Tail of pancreas > Spleen
39. In duodenal ulcer : Celiac nodes involved. T7-L1 supply Anterior abdominal wall
40. Tubular structure with absorptive area + lymphoid tissues is = Appendix
41. Endoderm gives rise to Endocrine pancreas. Greater splanchnic nerve supplies adrenal glands
42. Pulsatile mass in abdominal in patient with arterial disease is Aortic aneurysm – lies at L1-L3 > T12-L2
43. Ilioinguinal Nerve Is Not posterior to kidney. Psychomotor disturbance is related to IBS
44. Severe fluid loss from COLON can result in Metabolic acidosis + Hypokalemia
45. If all arteries supplying stomach are ligated, then = inferior pancreaticoduodenal will be spared
46. SMA is anterior to Lt renal vein , Lt renal vein crosses aorta (posteriorly aorta)
47. After multiple fractures 1 st step to manage is = Fluid replacement
48. Gastroduodenal artery lies posterior to 1 st part of duodenum
49. Phrenico colic ligament prevents downward displacement of spleen
50. First 2cm of duodenum supplied by Rt Gastric artery mainly
51. First part of duodenum by : Superior pancreaticoduodenal artery
52. Retrocecal appendix is the most common site. 65%. Liver biopsy at : T10 Mid Axillary Line
53. Defecation is initiated by Mass movement but carried by Sacral Parasympathetics

54. Defecation reflex is Rectoanal > Anorectal reflex. In child = Gastrocolic reflex
55. Cystic artery supplies proximal bile duct. Fenestrated capillaries mostly present in Kidneys
56. SMA Switched to IMA At= 2/3 rd Transverse Colon
57. Left nick at hepatoduodenal ligament will damage = hepatic artery
58. To Confirm Hypersplenism = Bone Marrow Aspiration is the best. For Splenomegaly : USG
59. Pancreas is derived from both dorsal and ventral primordium
60. Kidneys, Ovaries, Testes drain into : Para Aortic or Lumbar Nodes at L2
61. Prostate drains mainly into Internal iliac nodes and few vessels into external iliac
62. Upper 1/3 rd of vagina drains into = both External + internal iliac nodes
63. Middle 1/3 rd of vagina : Int iliac only ; Lower 1/3 rd drains into = superficial inguinal
64. Verge of anal canal drained by : Superficial inguinal nodes
65. Arteries at 2 & 10' O clock = Floch's arteries. At 5 & 7' o clock = Badenoch's arteries
66. Landmark in childbirth = ischial spine. T2 is the spinal level of PUJ
67. After RTA inc B.P that fluctuates is due to = inc Sensitivity to Catecholamines due to upregulated alpha receptors
68. After delivery , hematoma in broad ligament due to = Uterine artery injured
69. Behind bladder from lateral to Medial = USA → Ureter, S.vesicles , ampulla of Vas deferens
70. Vertical > Midline incision is preferred in Myomectomy
71. Genital branch of genitofemoral nerve passes through deep ring
72. Perineal membrane forms superficial boundary of superficial perineal pouch.
73. While sitting, we sit on = Ischial tuberosities
74. UV prolapse with Cervix at introitus = uterosacral Ligament damaged
75. External anal sphincter is anteriorly attached to = Perineal Body
76. Fall from height leads to Urinary incontinence in = lumbosacral segment lesion
77. Urogenital diaphragm is lateral to lower vagina. Levator anii is lateral to middle vagina
78. Ureter is lateral to Upper vagina. Middle rectal artery remains inside True Pelvis
79. External Urethral Sphincter Is present in = Urogenital diaphragm
80. Tubular structure with thick vascular wall + Pseudo str. epithelium = Vas Deferens
81. After pudendal nerve block urinary incontinence occurs due to = Ext Urethral Sphincter damaged
82. In Pelvic Outlet fracture = Acetabulum is intact. In pelvis fracture : Ischial Tuberosities are intact
83. Damage to perineal body damages = Bulbospongiosus muscle
84. Str. squamous epithelium, inc Vascularity & elasticity present in = Vagina
85. 18gm is the weight of normal prostate (choose 20, if 18 gm not given in options)
86. Scarpa fascia becomes continuous with membrane of Urogenital diaphragm
87. Uterine cancer spreads to Labia via Round Ligament of uterus
88. Skin of glans penis drains into superficial inguinal nodes. Levator anii forms medial wall of Ischiorectal fossa
89. Weight bearing line passes through ischial tuberosities. Main support of uterus = Transverse or lateral Cervical ligament
90. Micturition reflex integrated in sacral segment of spinal cord
91. After fall from height Urinary + bowel incontinence = Urethral rupture, Not Cauda Equina syndrome, As, in cauda equina syndrome saddle anaesthesia + loss of reflexes present along with bowel and bladder dysfunction
92. Prerenal fascia is an extension of renal fascia. Ovarian artery is direct branch of Abd aorta
93. Rt gonadal vessels lie anterior to IVC. Left gastric artery is not seen in Lesser omentum
94. Posterior duodenal perforation = contents go to lesser sac
95. Anterior duodenal perforation, contents go to = right posterior sub hepatic space
96. Diff b/w left, and right kidney is the Relations at Hilum
97. After Cholecystectomy place drain at Rt Subhepatic compartment. After Laparotomy drain placed at = right colic
98. Tumor at porta hepatis will compress Portal vein. Hepatoma will early compress Portal vein
99. Nick on right side at hepatoduodenal ligament = CBD damaged. Head of pancreas cancer will compress CBD
100. Pancreas is anteriorly bounded by Transverse colon. Small intestine is 6-8 metres long
101. Contents from caecum to ileum are prevented by ileocecal valve
102. Skin of scrotum drains into Superficial inguinal nodes. Pubococcygeus is a major part of levator anii
103. Splanchnic nerves > Hypogastric nerves supply Internal urethral sphincter
104. Wedge shaped fibromuscular mass separating Urogenital & anal triangle = Perineal body
105. Uterine artery passes anterior to Ureter. Sacral plexus supplies Piriformis & Obturator internus muscle
106. Pudendal nerve + Sacral S4 supply = Levator ani

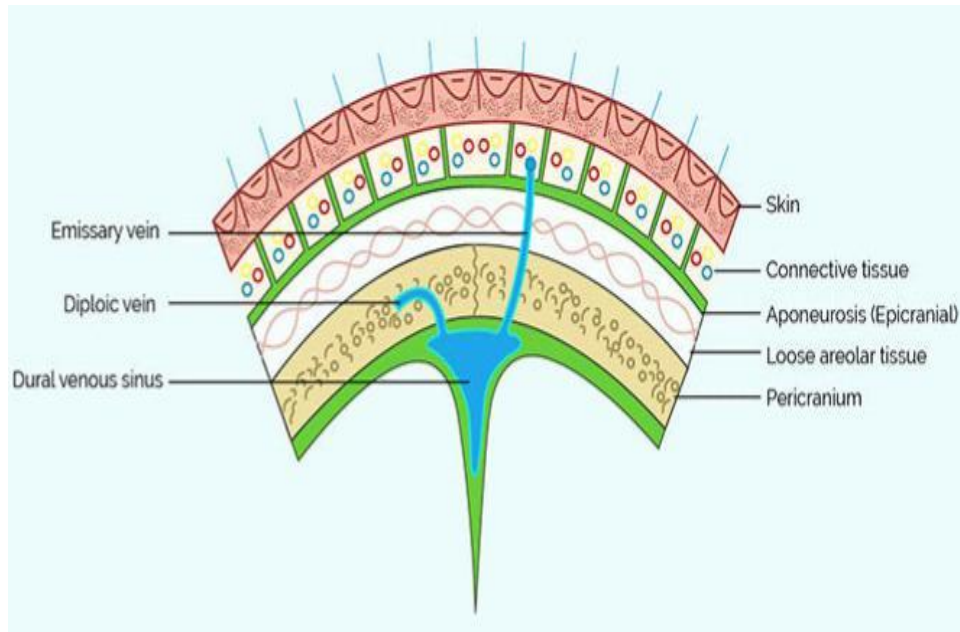
107. Anterior half of sphincter urethra covered by = Urogenital diaphragm. L. ani is main support of Pelvic viscera
108. Superficial inguinal nodes follow the path of Round Lig of uterus
109. Inferior rectal artery supplied lower third of rectum. Inferior phrenic artery is 1 st branch of abd aorta
110. Child with Unilateral hydronephrosis : obstruction at PUJ. Left renal vein is anterior to aorta and left renal artery
111. Highest Potassium or electrolyte loss by: Colon. T8-12 supply Midgut
112. Middle colic is involved in ischemia from Hepatic flexure to Mid transverse colon
113. Sigmoid colon begins at pelvic brim. Ampulla of Vater opens at posterolateral duodenum
114. Inferior rectal artery is branch of internal pudendal artery. Middle rectal from = Internal iliac Superior rectal from = IMA. Middle hepatic vein divides liver into Rt and left lobes. Falciform ligament divides Rt and left subphrenic spaces
115. Accessory Pancreatic duct drains = Upper Head > Uncinate process
116. Arcuate artery present at base of pyramid. Tunica vaginalis derived from – Parietal peritoneum
117. Needle passed to drain fluid from tunica vaginalis which layer not pierced = Tunica albuginea
118. Bladder vessels lie in bladder = Dorsolateral ligament
119. Common site of Ectopic pregnancy = Ampulla of Fallopian Tube ; Cervix- is least Common site
120. Fingers not Reachable to Sacral Promontory -Android Pelvis
121. Fingers Reachable to Sacral Promontory – Contracted Pelvis
122. Mediolateral episiotomy structure damaged is = Bulbospongiosus .
123. Mediolateral episiotomy structure at risk of damage = Levator ani
124. Median episiotomy structure damaged is : External anal sphincter
125. fallopian tube, Uterus & upper 1/3' of vagina are derived from = Paramesonephric duct
126. Urogenital Sinus forms = Lower Vagina
127. True Conjugate = Sacral Promontory to upper pubic Symphysis (11cm)
128. Obstetric Conjugate = Sacral Promontory to middle or posterior pubic Symphysis (10.5cm)
129. Diagonal Conjugate = Sacral Promontory to Lower pubic Symphysis (12cm)
130. During Hysterectomy Ureter Damage at = Cardinal Ligament > Behind Broad Ligament > At Pelvic Brim
131. Ureter Damage at Pelvic Brim While crossing = Common iliac Vessels
132. Anterior to Ureter = Gonadal Vessel ; Posterior to Ureter = iliac vessels
133. While removing ovary damage to structure = Ureter > Int iliac vessels
134. Common Site of Lodging of ureteric stones overall Adults = Vesico ureteric Junction VUJ
135. Common Site of Lodging of ureteric stones in Child Pelvic ureteric Junction PUJ
136. Ureter Narrows at = Vesico ureteric Junction > Where it enters Bladder
137. Uterus Prolapse: 1 st Degree – Decent of Cervix within Vagina ; 2 nd Degree -Decent of Cervix to Introitus ;
138. 3 rd Degree -Decent of Cervix Outside Introitus ; 4 th Degree(Procidentia)- Whole Uterus outside Introitus
139. In 1 st – 3 rd Degree prolapse : Uterosacral Ligament Damage
140. 3 rd Degree- Uterosacral > Cardinal Ligament Damage. 4 th Degree – Cardinal Ligament Damage
141. Neck of female urethra lies above urogenital diaphragm & Female urethra more prone to infection
142. External urethral meatus = Narrowest part of urethra. Prostatic urethra – widest and most distensible
143. Membranous urethra : Shortest and least dilatable urethra
144. Bulbar Urethra Rupture (Below Urogenital Diaphragm) urine into = Superficial Perineal Pouch
145. Membranous Urethra Rupture(At Urogenital Diaphragm) urine into = Deep Perineal Pouch
146. Prostatic Urethra Rupture(Above Urogenital Diaphragm) urine into = Retropubic Space
147. Penile Urethra Rupture Urine into = Scrotum > Anterior Abdominal Wall
148. Contents of deep perineal pouch include = Dorsal nerves of penis/ clitoris , Deep transverse perineal muscles Bulbourethral glands , Internal pudendal vessels and branches, sphincter urethrae , membranous urethrae
149. Contents of Superficial Pouch include = Perineal body , root of penis / Clitoris, Bulbospongiosus,
150. ischiocavernosus, superficial transverse perineal muscles , Perineal branch of Pudendal nerve.
151. Internal anal sphincter supply = Sympathetic(L1-2) and Parasympathetic(S2-4) through hypogastric plexus
152. External anal sphincter supply = Inferior rectal branch of pudendal nerve(S2-4) and perineal branch of S4
153. Above Pectinate line anal canal supply = Sympathetic(inferior hypogastric L1, L2) and Parasympathetic(S2-S4)
154. Below Pectinate line anal canal supply = Somatic(Inferior rectal-S2-4)
155. Internal urethral sphincter supply = Parasympathetic pelvic splanchnic nerve(S2-4)
156. External urethral sphincter (sphincter urethra) supply = Pudendal nerve(S2-4) causes Control over Micturition
157. Regarding Bladder, Peritoneum covers superior and upper part of posterior surface rest all surfaces devoid of peritoneum
158. Motor supply of bladder by both sympathetic and Parasympathetic

159.Sympathetic through hypogastric nerve (T1-L2) cause relaxation of detrusor muscle (Urine Retention)
160.Parasympathetic- Through pelvic splanchnic nerve (S2-4) Cause contraction of detrusor muscle
161.Pain Sensation of bladder pass through- Lateral Spinothalamic tract
162.Awareness of Bladder distension mediated by DCML(Posterior Column)
163.Pain and filling sensation of bladder by Sympathetic system
164.Regarding Rectum , Sympathetic(L1-2) & Parasympathetic(S2-4) through superior rectal (inferior mesenteric) and Inferior Hypogastric plexuses. Distension of rectum carried by – Parasympathetic.
165.Pain of Rectum carried by -Sympathetic and parasympathetic
166.Remnant of Gubernaculum in female: Upper Part- Round ligament of ovary ; Lower Part – Round ligament of Uterus
167.Remnant of Gubernaculum in male : Upper Part- Degenerate ; Lower Part (Gubernaculum Testis) Scrotal ligament.
168.T12- Celiac Trunk ; L2 -Renal Artery ; L1 Superior mesenteric artery ; L3 Inferior Mesenteric Artery
169.At Transpyloric Plane – Pylorus of Stomach, Fundus of Gallbladder, Hilum of Kidney, First Part of Duodenum, Origin of SMA, Tip of 9 th Costal Cartilage, Lower end of Spinal Cord.
170.Right Kidney anteriorly Related to Liver whereas Right Kidney Hilum Anteriorly Related to 2nd Part Duodenum
171.Posterior to Right Kidney -12 th Rib & Diaphragm
172.Anterior to Left Kidney – Stomach & Pancreas & Posterior to Left Kidney are 10 th , 11 th Ribs & Diaphragm
173.Anterior to Right Suprarenal gland → IVC + Rt lobe of Liver. Posterior to Right Suprarenal gland -Diaphragm
174.Anterior to Left Suprarenal gland – Pancreas , Lesser sac, and stomach & Posterior to Left Suprarenal gland -Diaphragm
175.2 nd Part of duodenum Attached posteriorly to Transverse Mesocolon
176.Right Accessory Hepatic Artery Branch of-SMA
177.Superficial Epigastric Artery is Branch of Femoral Artery & Superior Epigastric Artery Branch of intern Thoracic Artery
178.Inferior Epigastric artery is branch of External iliac artery
179.External Spermatic Fascia from external oblique. Internal Fascia from fascia transversalis
180.cremasteric fascia from internal oblique. Direct inguinal hernia occurs at – Hesselbach triangle
181.Surgeon performing in inguinal hernia repair structure seen = Pampiniform plexus
182.Deep inguinal ring formed by Fascia Transversalis
183.Superficial ring formed by opening external oblique aponeurosis
184.Superficial ring traversed by ilioinguinal nerve
185.Inguinal hernia above and medial to pubic tubercle. Direct Hernia medial to- Inferior epigastric artery
186.Indirect hernia lateral to – Inferior epigastric artery. Inferior epigastric artery lateral to Direct hernia
187.Inferior epigastric artery medial to – Indirect inguinal hernia. Femoral hernia below and lateral to public tubercle
188.In Femoral Sheath most lateral structure is structure is Genital branch of femoral nerve > Femoral artery
189.Femoral hernia descends behind inguinal ligament. Medial to femoral hernia = Lacunar ligament
190.Bare area of liver limited by- Coronary ligament
191.Lacunar Ligament formed by = Inguinal ligament extension
192.Congenital diaphragmatic hernia is due to = Defective Or incomplete pleuroperitoneal membranes
193.Right adrenal gland separated Stomach from kidney by perinephric Fat
194.During Esophagectomy stomach mobilized up in thorax , now artery to be used is = Rt Gastroepiploic artery > Rt gastric
195.Giving incision at McBurney's point= iliohypogastric nerve + Deep Circumflex artery injured
196.Pain of appendix felt at umbilicus through T10 Sympathetic
197.Left gastric artery arises from – Celiac trunk & Right gastric from – Hepatic artery. Short gastric from- Splenic
198.Left Gastroepiploic from Splenic artery and Right Gastroepiploic from – Gastroduodenal artery
199.Most Common location of Duodenal Ulcer – 1 st part of Duodenum
200.Perforation of posterior wall of duodenum Bleed by – Gastro duodenal artery
201.Most common location of gastric ulcer near – incisura angularis on Lesser curvature.
202.Perforation of lesser curvature Bleed by – Left gastric artery
203.Perforation of posterior wall of stomach Bleed by – Splenic artery
204.Interlobar artery passes in between medullary pyramid and at the base of pyramid it turns, run parallel to base of pyramid, and form Arcuate artery.
205.Renal columns have- Interlobar Artery. Capsule & Glomerulus Contain – Interlobular Artery
206.Hilum Contain Segmental Artery
207.Coccygeal ligament is extension of Dura matter starts at S2 and ends at Coccyx
208.Tumor in deep perineal space may affect bulbourethral glands. Dorsal vein of penis drains into Santorini Plexus
209.Superficial vein of penis drains into Saphenous vein
210.Ejaculatory duct opens into Prostatic utricle. Ducts of Cowper's glands open into Penile Urethra

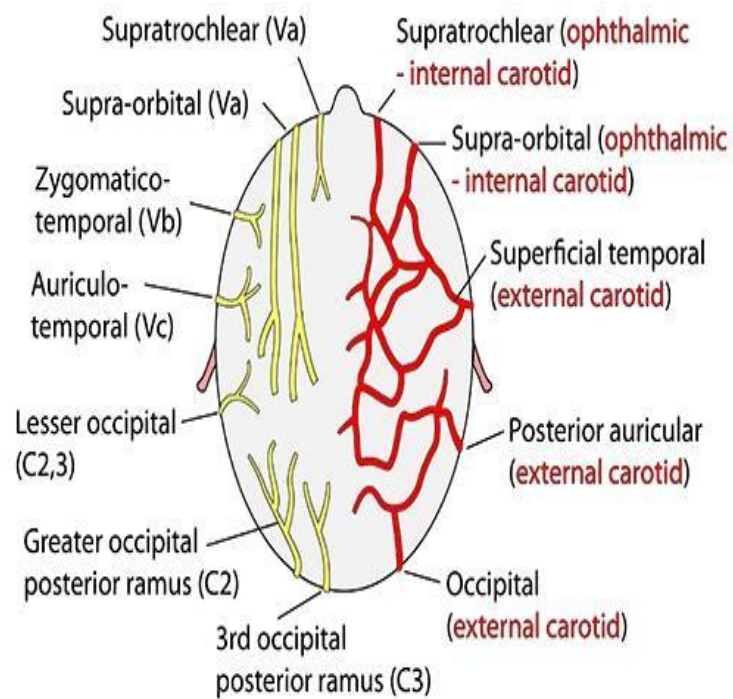
211.Seminal vesicles open with ejaculatory ducts into prostatic urethrae
212.Embryological counterpart of mullerian tubercle is Seminal colliculus
213.Uterine + Ovarian arteries supply uterus
214.For Culdocentesis = Posterior fornix of vagina is used
215.Internal iliac nodes involved in cervical cancer (stage 4)
216.Adjacent spinous processes of Sacrum fuse to form : Median Sacral Crest
217.Failure of fusion of S4 , S5 = Sacral Hiatus formation
218.Urogenital diaphragm attaches laterally to inferior ischiopubic rami
219.In Prostatectomy --- Denonviller's Fascia is preserved
220.After Total hysterectomy , normal saline used for washing touches pelvic brim goes to → Subphrenic space
221.Psoas muscles arises from Lumbar region and go towards deep pelvis
222.Stone at PUJ = T12 – L2 level. On DRE, anterior surface of Coccyx is palpable
223.Internal iliac cut at origin will spare Scrotum > Penis
224.PIRIFORMIS is present in greater sciatic foramina.
225.Urine accumulation in scrotum ,Ant Abd wall = Spongy or Penile urethrae ruptured
226.Anatomically, peripheral zone is the largest zone of prostate, while lateral lobe – largest lobe
227.Damage to Pubic symphysis will damage = Levator Anii > Rectum (posteriorly)
228.Prostatic ducts open into Seminal colliculus > prostatic sinuses
229.Cervix is palpable on PV Exam. Neck of female urethra lies ABOVE the Urogenital diaphragm
230.In GYNAECOID PELVIS : AP diameter is shorter than TRANSVERSE diameter
231.Injury Inferolateral to pubic tubercle damages Obturator nerve
232.Bulbar urethrae lies is Superficial pouch. Inferior Vesical artery supplies prostate
233.Pain in thigh in Ca rectum = sacral nerves involvement. Vagina has abundant ELASTIC fibres only
234.Internal pudendal artery enters pelvis via Lesser Sciatic foramina and leaves via Greater sciatic foramina
235.Ureter Opens as OBLIQUE SLIT In bladder
236.Loss of cutaneous sensations at urogenital area → Pudendal nerve lesion. If asked which one is spared = iliohypogastric
237.Bicornuate uterus associated with RENAL anomalies
238.Meckel diverticulum : Rule of 2 ; Seen commonly in under 2-year , 2% Population , 2 Feet proximal to ileocecal valve , 2 inches long , Types of mucosa (Ectopic gastric mucosa which usually bleed and Pancreatic mucosa
239.Ventral mesogastrium derivatives: <ul style="list-style-type: none"> o Falciform ligament → Connect Liver to Anterior abdominal wall , o Hepatoduodenal ligament: Contains Portal triad: proper hepatic artery, portal vein, common bile duct o Gastro hepatic ligament → Contains Gastric vessels.
240.Dorsal mesogastrium Derivatives <ul style="list-style-type: none"> o Gastrosplenic ligament : Connect greater curvature and spleen, Contain Short gastric, left gastroepiploic o Gastrocolic ligament : Connect greater curvature and Transverse colon -- Contain Gastroepiploic arteries o Splenorenal ligament -- Connect Spleen to left Para renal space , Contain Splenic vessel, and tail of pancreas
241.Epiploic foramen (Winslow's foramen is a passage between greater and lesser sac.
242.Boundaries Posteriorly = IVC
243.Lumbar triangle (of petit) – the common site of Hernia in abdomen, especially inferior triangle. <ul style="list-style-type: none"> o Anterior boundary by Post border of external oblique. o Posterior boundary by Anterior border of latissimus dorsi o Floor -Internal oblique , while Below it is formed by – Iliac crest
244.Posterior to Uncinate process –Aorta and Anterior to uncinat process = SMA
245.Posterior to neck of pancreas- Portal vein and SMV
246.Superior to pancreas Splenic Artery. Most abundant cells in Pancreas = B cells (insulin)
247.Islets abundant in = tail of pancreas
248.Below arcuate line, Rectus sheath is deficient posteriorly as rectus muscle lies directly on fascia transversalis
249.Most common hernia overall in both female + Male = indirect Inguinal hernia
250.Femoral hernia more common in females and prone to be strangulated due to narrow neck / sac of hernia.
251.Puborectalis forms sling around anus, relaxation of it helps in defecation
252.Pelvic outlet bounded anteriorly by Urogenital diaphragm
253.Middle rectal artery > lateral sacral is congenitally sometimes absent.
254.Superficial external pudendal emerges from Saphenous Opening.

HEAD & NECK ANATOMY

SKULL		
Bones	<ul style="list-style-type: none">Skull has 22 bones excluding the ossicles of ear.Bones of infant’s skull are more resilient than the adult, so, more prone to fractures.Paired bones -Temporal ,Parietal , Nasal, Palatine, Lacrimal Zygomatic, Maxillae, Inferior Nasal Conchae.Unpaired - Frontal, Sphenoid, Ethmoid, Occipital Bones, mandible, and, Vomer.Nasal bone is the most common facial bone to be fractured followed by Zygomatic (2nd).zygomatic bone (cheekbone or malar bone) is a paired bone.The single frontal bone forms the Forehead.Inion is the most prominent projection of the protuberance which is located at the Posteroinferior (lower rear) part of the human skull.Pneumatic bones : irregular bone containing large air spaces lined by epithelium e-g. Sphenoid, Ethmoid, Maxilla, and mastoid.Mastoid process of temporal is absent at birth. Thinnest orbital wall is the medial wall.Glabella: area between eyebrows just above nose or frontal bone between superciliary archesVault is bigger than face in children.Parts of 7 bone contributes to the bony framework of each orbit of eye.	
Sutures	<ol style="list-style-type: none">Coronal suture: between the frontal and parietal bones.Sagittal suture: between the paired parietal bones.Lambdoid suture: between the parietal and occipital bones.Metopic suture separates the 2 frontal bones at birth- 1st skull suture to close physiologically. <ul style="list-style-type: none">Order of sutures closure = Metopic > Sagittal > Coronal > Lambdoid suture	
Fontanelle	<ol style="list-style-type: none">Anterior Fontanelle or Bregma:<ul style="list-style-type: none">Lies B/w 2 halves of frontal bones and two Partial bones.diamond shaped and closed by 18 months of age.Heart rate, intracranial pressure and degree of dehydration can be examined by palpating the anterior fontanelle. Anterior is larger than posterior fontanelle.Posterior Fontanelle or Lambda triangular shaped, between the 2 parietal bones and occipital bone it is closed by the end of first year (12 months)	
SCALP		
Layers of Scalp	Mnemonics = SCALP <ul style="list-style-type: none">S- Skin contain hairs and it is the first layer.C- Connective tissue (dense-second layer), contains arteries, veins and nerves supplying scalp.A- Aponeurotic layer contains occipitofrontalis muscle.L- loose Areolar connective tissue, contains emissary vein and that's why it is the danger areablackening of eye, infection of scalp spread through this layer (4th layer)P – Pericranium is the 5thlayer	
Blood & Nerve supply	Blood supply <ol style="list-style-type: none">Supra orbital arterySupra trochlear arterySuperficial temporalPosterior auricularOccipital artery	Nerve supply (GLASS) <ul style="list-style-type: none">Greater occipital & Greater auricular N.Lesser occipital nerveAuriculotemporal nerve- to supply the temporal scalp.Supratrochlear- supplies foreheadSupraorbital.
Lymphatics	No lymphatics present in scalp	
Clinical anatomy	<ul style="list-style-type: none">Blood supply is present in second layer(dense connective tissue), Or we can say it is between the skin & Aponeurotic layer.Danger area of face is the fourth layer (Loose areolar tissue layer).Cephalohematoma most common site is the Parietal bones.It is Present b/w scalp & Periosteum or sub periosteal, Prefer Subperiosteal > Parietal bones	



SCALP - ARTERIES AND NERVES



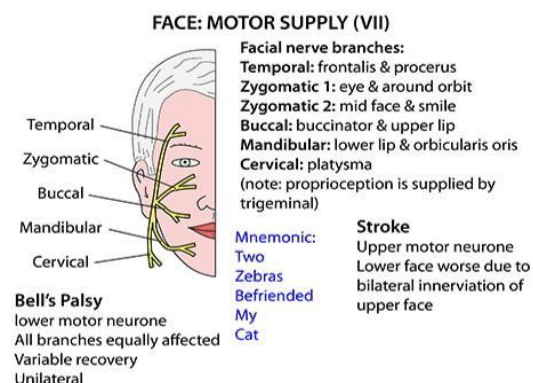
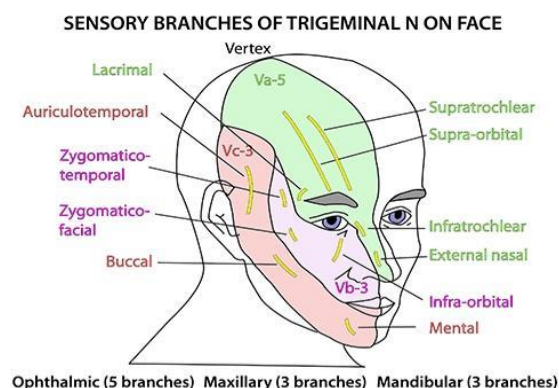
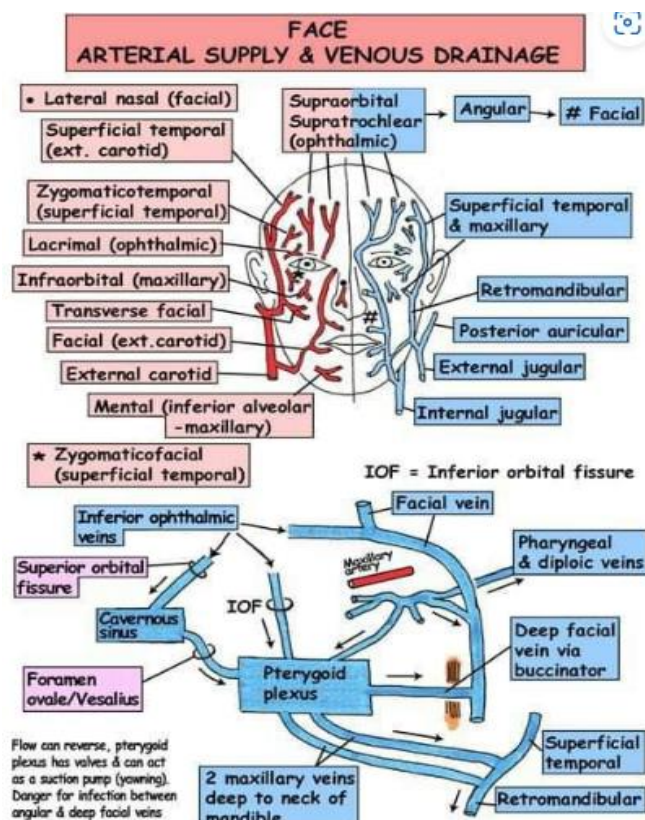
SKULL FORAMINA	CONTENTS
Foramen Cecum	Nasal emissary vein to superior sagittal sinus
Foramen Lacerum	Meningeal branch of ascending pharyngeal artery, greater petrosal nerve, emissary veins connecting the extracranial pterygoid plexus with intracranial cavernous plexuses
Optic canal	Optic nerve and Ophthalmic artery with central retinal branch
Superior orbital fissure	The superior narrow lateral part of fissure: ophthalmic nerve, lacrimal nerve, frontal nerve, trochlear nerve, superior ophthalmic vein (to cavernous sinus)- involved in spread of infection from danger area of face. Inferior wide medial part of fissure: Abducent nerve, nasociliary nerve, Oculomotor nerve Through the superior orbital fissure: orbital branches of middle meningeal artery, one of the two branches of inferior ophthalmic vein (the other is infraorbital vein) and, ophthalmic nerve.
Zinn's ring	Zinn's or common tendinous ring surrounds optic canal and inferior part of superior orbital fissure. Through it, Optic nerve, Ophthalmic artery, Abducent nerve, nasociliary & Oculomotor nerve pass
Inferior orbital fissure	Infraorbital nerve + artery & Vein (infraorbital vein is branch of inferior ophthalmic vein) Zygomatic nerve, orbital branches of pterygopalatine ganglion, terminal branches of anterior temporal artery
Foramen Ovale	MALE = Mandibular nerve, accessory meningeal artery, lesser occipital nerve, Emissary vein
Foramen Rotundum	Maxillary nerve (CN V2)
Foramen Spinosum	Middle meningeal artery & vein, Meningeal branch of mandibular nerve
Internal auditory meatus	In superior part: Facial nerve (with its main sensory division-Nervus intermedius) In inferior part: Vestibulocochlear nerve (cochlear part- anteriorly, vestibular part- posteriorly)
Carotid canal	Internal carotid artery, carotid sympathetic plexus
Jugular foramina	Anterior part: Glossopharyngeal nerve, inferior petrosal sinuses Middle part: Vagus + accessory nerve, meningeal branch of occipital artery Posterior part: Sigmoid sinus, superior bulb of jugular vein In short, CN 9, 10, 11, IJV, sigmoid + inferior petrosal sinus
Foramen Magnum	Medulla oblongata with meninges, Vertebral artery with meningeal branches, 1 anterior spinal artery, two posterior spinal arteries, emissary veins to basilar plexus, spinal accessory nerve, Ascending sympathetic fibres, apical ligament, and tectorial membrane

FACE

- No deep fascia is present in **Face**.
- Skin of face has numerous sweat & sebaceous glands.
- It is connected to underlying bones by loose C.T, in which are embedded the muscles of facial expression.
- Buccinator and superior constrictor arise from pterygomandibular raphe.

Blood supply	<ul style="list-style-type: none"> ○ Facial artery, Superficial temporal, Transverse facial, Infra orbital, lacrimal, Zygomaticofacial, Zygomaticotemporal, Supra trochlear and Supra orbital arteries
Venous drainage	<ul style="list-style-type: none"> ○ Facial Vein is formed at the medial angle of eye by supraorbital + supratrochlear veins. ○ It descends behind the facial artery to the lower border of body of mandible. ○ it is connected to cavernous sinus through superior ophthalmic vein ○ This connection is of great clinical importance because it provides a pathway for spread of infection from face to cavernous sinus ○ It is joined by anterior division of retromandibular vein to form common facial vein to end into the internal jugular Vein
Nerve supply	<ul style="list-style-type: none"> • Sensory via Trigeminal nerve (CN V) while motor via Facial nerve (CN VII)

	<ul style="list-style-type: none"> ○ Sensory supply by branches of trigeminal nerve except the area over the angle of mandible and the parotid gland, which is supplied by great auricular nerve. ○ Main branches of Trigeminal nerve → Ophthalmic N, maxillary N, and, mandibular N. ○ Motor Supply of face is by Facial Nerve via following branches: <ul style="list-style-type: none"> ✚ Temporal, Zygomatic, Buccal, marginal mandibular and Cervical branch (supplies platysma) ✚ Marginal mandibular branch is commonly injured in submandibular gland surgeries
Lymphatic drainage	<ul style="list-style-type: none"> ● Lymph from forehead + anterior part of face drains into -- Submandibular L.Ns. ● Lateral part of face + lateral parts of eyelids drain into -- parotid L.Ns. ● Lower lip + chin --- drained into Submental L.Ns.



Mandible

- Largest and strongest bone of the face. 2nd bone after clavicle to ossify in the body.
- Each half of mandible ossifies from one centre which appears in the 6th week of intrauterine life.
- **2 types of ossification are seen in the mandible.**
- The **mental foramen can be seen below the 2nd premolar teeth.**
- This foramen Transmits mental nerve and vessels. With aging , the foramen moves Up.
- Pressure on mental nerve can cause numbness of lower lip.
- Inferior alveolar nerve and vessels enter mandibular canal through mandibular foramen.
- Inferior alveolar nerve supplies all lower jaw teethes, lower lips, Buccal mucosa from the Incisor to the premolar and the skin over the chin.
- Mandibular canal contains the inferior alveolar nerve, artery & vein,
- Mylohyoid groove transmits Mylohyoid nerve and vessels.
- Mandibular fractures are typically the result of trauma.
- The most common area of fracture is at the condyle > body > angle > Symphysis
- **Mandibular fracture just before the mandibular foramen will cause loss of sensation of Lower jaw, lower teeth, and lower lip due to damage to inferior alveolar nerve**

Temporo-mandibular joint (TMJ)	<ul style="list-style-type: none"> ○ Hinge type synovial joint. Fibrocartilage divides the joint into upper and lower cavities ○ Capsule enclose the joint Ligaments: <ol style="list-style-type: none"> 1. Stylomandibular ligament Formed by deep part of parotid fascia 2. Sphenomandibular ligament is the derivative of 1st arch 3. Lateral ligament or Temporomandibular ligament: The thick part of the articular capsule forms the intrinsic lateral ligament (Temporomandibular ligament) which strengthens the TMJ laterally. ● It Acts to Prevent posterior dislocation of the joint <p>Nerve supply: Auriculotemporal nerve is the Sensory supply of capsule of TMJ, also Masseter nerve</p> <p>Blood supply: Superficial temporal artery</p> <p>Clinical Anatomy & Key Facts</p> <ul style="list-style-type: none"> ▪ TMJ dislocation occurs during extreme opening of mouth (e.g., yawning) as the sudden contraction of lateral pterygoid muscle may be sufficient to pull disc forward beyond the summit → dislocation ▪ Except for the Geniohyoid muscle, which is innervated by the C1 spinal nerve, all muscles that move TMJ are innervated by mandibular nerve branches that originate in the infratemporal fossa. ▪ TMJ dislocation occurs when the condyle of jaw moves forward, out of its functional position within the glenoid fossa and posterior articular eminence so that the condyle is anterior to the eminence
Muscles of Mastication	<ul style="list-style-type: none"> ○ They develop from first arch and innervated by mandibular nerve. ○ Medial pterygoid muscle Elevates the mandible to close mouth. ○ Lateral pterygoid muscle is the only muscle that OPENS Mouth by depressing the Mandible and mostly damaged during TMJ dislocation. ○ Lower head of lateral pterygoid enters between both heads of the medial pterygoid. ○ The articular disc of TMJ is developmentally a part of tendon of lateral pterygoid muscle. ○ Temporalis muscle: Elevates the mandible, closing the mouth. Also retracts the mandible, pulling the jaw posteriorly. ● It Arises from the temporal fossa and the deep part of temporal fascia. ● It passes medial to the zygomatic arch and forms a tendon which inserts onto the coronoid process of the Mandible. ○ Masseter muscle is the most powerful muscle of mastication. ○ The pterygoid venous plexus is occasionally known as a peripheral heart for during yawning when the mouth is broadly open because of contraction of lateral pterygoids

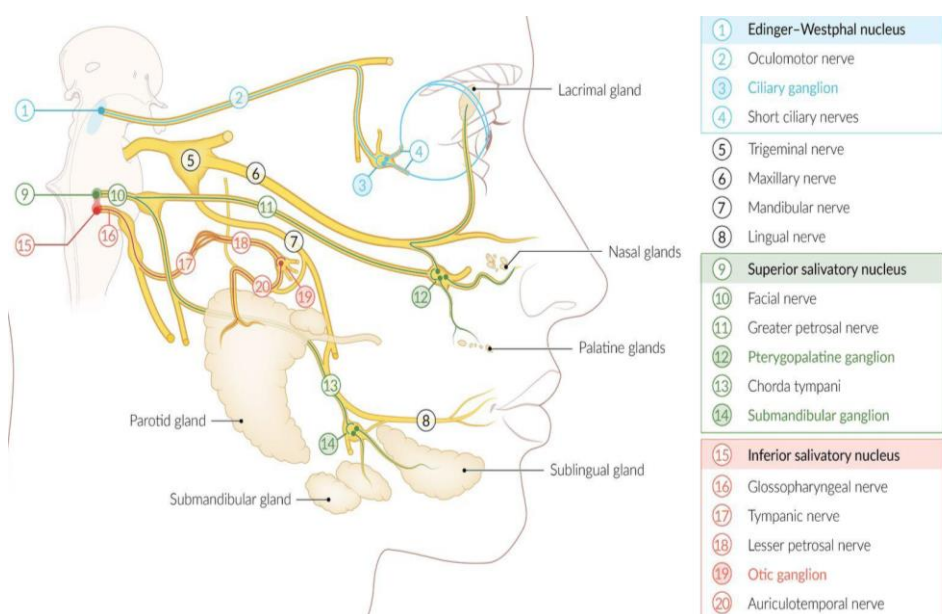
RULES FOR NERVE SUPPLY OF MUSCLES

➤ All muscles of face are supplied by facial nerve except Levator palpebrae superioris (by Oculomotor nerve)
➤ All muscles of mastication are supplied by mandibular division of trigeminal nerve.
➤ All muscles of tongue supplied by hypoglossal nerve except palatoglossus muscle (by pharyngeal plexus)
➤ All muscles of pharynx supplied by Pharyngeal plexus except stylopharyngeus (by Glossopharyngeal nerve)
➤ All muscles of palate supplied by Pharyngeal plexus except tensor veli palatini (by nerve to medial pterygoid muscle)
➤ All muscles of larynx supplied by recurrent laryngeal nerve except cricothyroid (external branch of superior laryngeal N)
➤ Pharyngeal plexus is made of fibres from glossopharyngeal + vagus nerve with sympathetic fibre.

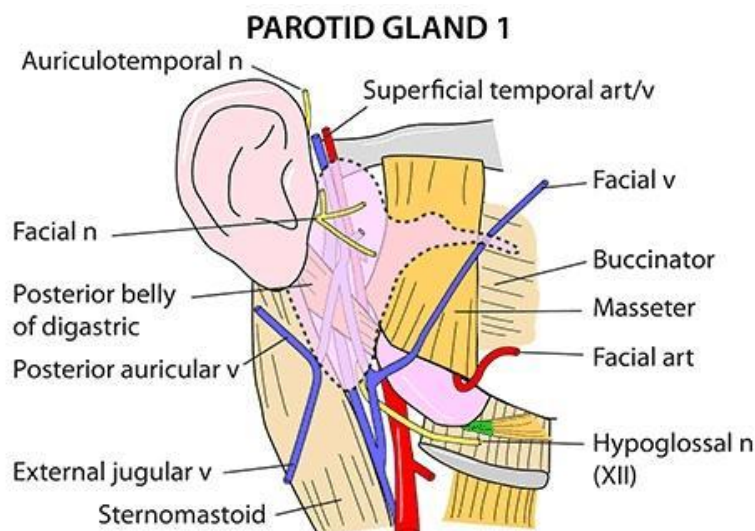
PTERYGOPALATINE FOSSA

Boundaries	<ul style="list-style-type: none"> ● Inverted Tear shaped immediately behind the Maxilla bone. ● Anterior: posterior Surface of maxilla. ● Posterior: pterygoid Process. ● Medial: Perpendicular plate of Palatine bone. ● Lateral: Infratemporal fossa (through Pterygomaxillary Fissure) ● Superiorly: greater Wing of sphenoid
Contents	<ul style="list-style-type: none"> ● Maxillary Nerve with branches, 3rd part of Maxillary artery and Sphenopalatine ganglion
Communications	<ul style="list-style-type: none"> ● Pterygomaxillary Fissure → Infratemporal fossa. ● Foramen rotundum → Middle cranial fossa.

	<ul style="list-style-type: none"> • Sphenopalatine Foramen. → nasal Cavity. • Inferior orbital fissure → Orbital cavity. • Greater palatine canal → Palate. • Palatovaginal canal → nasopharynx • Pterygoid canal. → Foramen lacerum
Contents of Infratemporal fossa	
Pterygoid venous plexus , Pterygoid muscles , Mandibular nerve & branches ,insertion of temporalis , Otic ganglion , Chorda tympani , Maxillary artery & branches , Posterior superior alveolar nerve	
MAIN PARASYMPATHETIC GANGLIA OF HEAD & NECK	
Ciliary ganglion	<ul style="list-style-type: none"> • Edinger Westphal nucleus → Pre-ganglionic via Oculomotor nerve & Post-ganglionic via Short ciliary nerves supply Sphincter papillae and ciliary Muscles. • Sensory and Sympathetic root via Nasociliary nerve
Otic ganglion	<ul style="list-style-type: none"> • Located just below Foramen Ovale deep to mandibular trunk. • Inferior Salivatory Nucleus → pre-ganglionic parasympathetic via Lesser Petrosal and Post ganglionic via Auriculotemporal nerve to Parotid gland • Sensory via Mandibular nerve (Motor) • Sympathetic through Plexus around Middle Meningeal artery → external petrosal nerve
Sphenopalatine or pterygopalatine ganglion	<ul style="list-style-type: none"> ○ Located in Pterygopalatine fossa suspended from Maxillary nerve. ○ Superior Salivatory Nucleus → Greater Petrosal Nerve + deep Petrosal nerve- join to form Vidian nerve/nerve of Pterygoid canal. ○ Post ganglionic Joins Maxillary Nerve to supply Nose , palate , Lacrimal gland, glands of Pharynx and oral cavity. ○ Sensory Root is via Maxillary nerve ○ Sympathetic Root : Deep petrosal nerve from plexus around internal carotid artery ○ This ganglion is involved in runny nose , hay fever & lacrimation or tears
Submandibular ganglion	<ul style="list-style-type: none"> ○ Located superficial to Hyoglossus muscle suspended from Lingual nerve ○ Superior Salivatory Nucleus → Pre-ganglionic via Chorda tympani branch of facial nerve, which joins lingual nerve to directly supply the Submandibular + Sublingual gland ○ Sensory supply by lingual nerve ○ Sympathetic fibres from Plexus around Facial artery
Key Facts	<ul style="list-style-type: none"> ○ Above 4 ganglia are anatomically related to Trigeminal nerve but functionally linked to the other cranial nerves ○ Superior Salivatory Nucleus → Submandibular + Sphenopalatine ganglion ○ Inferior Salivatory Nucleus → Otic ganglion (Glossopharyngeal nerve)

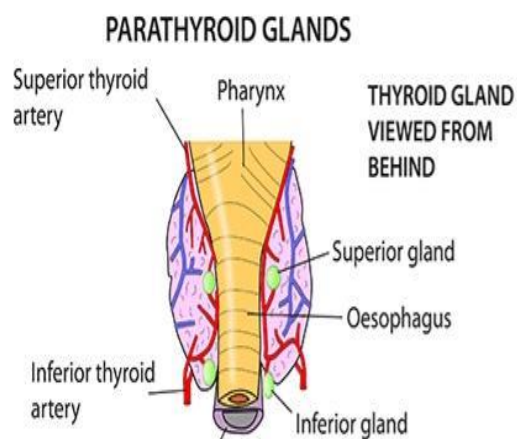
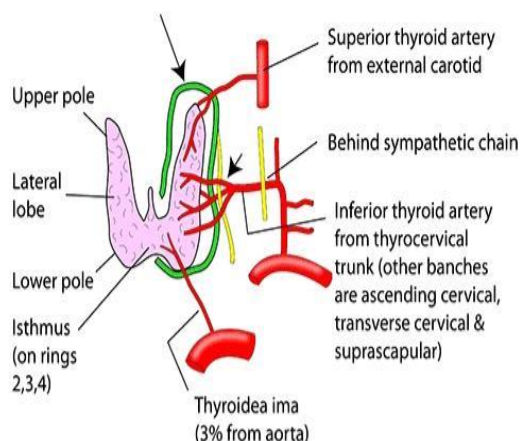


SALIVARY GLANDS	<ul style="list-style-type: none"> • Three major salivary glands (parotid, submandibular, sublingual gland) and numerous minor salivary glands present in oral cavity • Nerve damaged during submandibular gland surgery: Marginal mandibular branch of facial nerve > lingual nerve > hypoglossal nerve • The percentage of salivary stones seen in submandibular gland is 80 % • Major amount of saliva (when salivary gland are not stimulated) are contributed by submandibular • Most common site of origin of pleomorphic adenoma is Parotid gland. • Most common site for carcinoma of oral Cavity is Lateral border of Tongue. • Most common malignant tumour of submandibular salivary gland is adenoid cystic carcinoma, which has a tendency for perineural invasion. • Common cause of salivary gland atrophy is the obstruction of excretory duct • Salivary glands have dual autonomic supply but not reciprocal supply
Parotid gland	<ul style="list-style-type: none"> • Largest among salivary gland, secretion is rich of amylase. • The Posteromedial surface of parotid gland is closely related to carotid fascia. • Secretory epithelium of parotid gland is derived from endoderm • Parotid produces Pure serous Saliva • Stensen duct: The parotid duct passes anteriorly across the external surface of the Masseter muscle and then Turns medially to penetrate the Buccinator muscle of the cheek and open into the oral cavity Adjacent to the crown of the second upper molar tooth. • Obstruction of duct will cause shrinking of parotid gland due to apoptosis • Structure from lateral to medial: FRE : Facial nerve (most superficial) , Retromandibular vein, ECA (most medial) • Frey's Syndrome is a syndrome that includes sweating and facial flushing while eating (gustatory sweating) caused by injury Auriculotemporal nerve typically after surgical trauma (e.g., superficial parotidectomy). • Lacrimation while eating → facial nerve involved. • Sweating after eating → auriculotemporal nerve involved.
Submandibular gland	<ul style="list-style-type: none"> • It is divided by Mylohyoid muscle into superficial and deep parts • The submandibular duct emerges from the medial side of the deep part of the gland in the oral Cavity and passes forward to open on the summit of a small sublingual papilla beside the base of Frenulum of the tongue • The submandibular duct or Wharton duct is the most common site for sialolithiasis. • Saliva produced by this gland is mixed - Serous & Mucoïd.
Sublingual gland	<ul style="list-style-type: none"> • Produces Pure Mucoïd secretions (More Mucoïd > little serous, but not Mixed). • Duct opens on the side of frenulum of tongue
Minor salivary glands	<ul style="list-style-type: none"> • About 800 glands in Submucosa of Oral Cavity > Lamina Propria. • Lingual Glands: Anterior (serous secretions) , middle (mixed) , posterior (mucous) • Buccal Glands: Mixed • Labial Glands : Mixed • Palatine Glands: mucous secretions

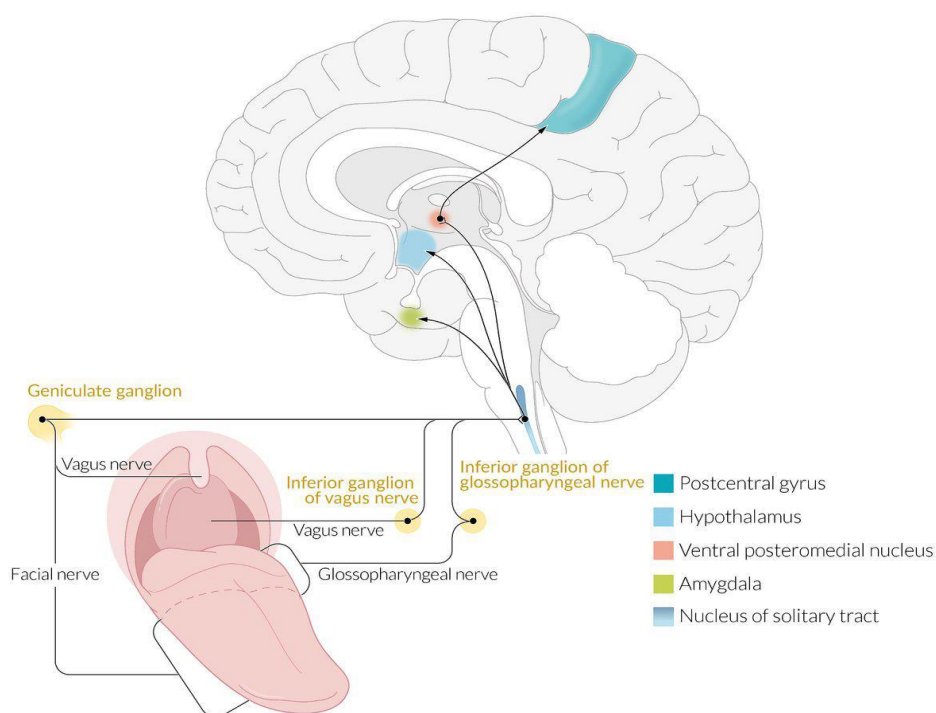


**Lies between mastoid, styloid process, ramus of mandible.
Surrounded by parotid fascia (investing layer of deep fascia)**

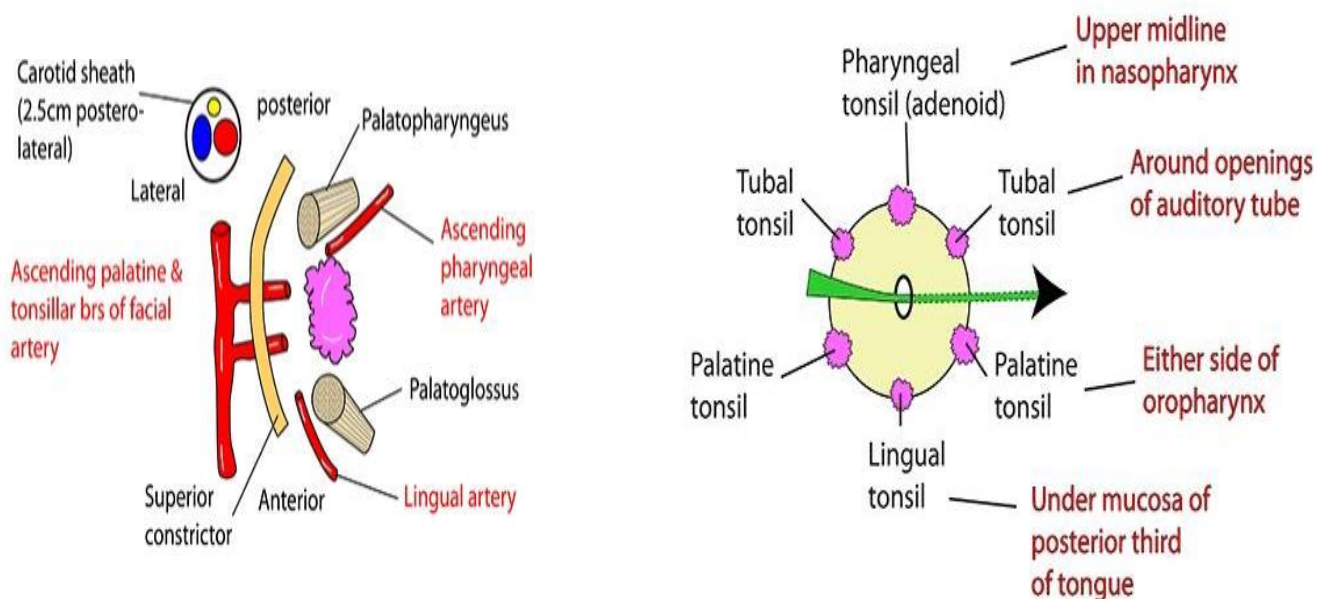
Thyroid gland	<ul style="list-style-type: none"> Bilobed, lobulated, 5cm long, extending to tracheal ring 6 and Shield shaped that lies on carotid sheath. Limited extension upwards by sternothyroid but can pass inferiorly into mediastinum Gland Extends from C5 – T1 Isthmus lies against 2nd – 4th Tracheal rings Blood supply via Superior thyroid (from ECA), inferior thyroid arteries (from Thyrocervical trunk) Thyroid Ima artery (3 % cases) arises from brachiocephalic > subclavian artery Venous drainage: Superior and Middle thyroid veins drain into IJV inferior thyroid vein drains into → Brachiocephalic veins Lymph drainage : Deep Cervical Nodes (Upper & Lower) ; isthmus drains into Brachiocephalic nodes Relations: Posterior: Prevertebral fascia, carotid sheath, parathyroid glands, trachea Posterolaterally : Carotid Sheath Medial: Recurrent laryngeal nerve, trachea, larynx, oesophagus Anterior: Pretracheal fascia, sternohyoid, sternothyroid Clinical Anatomy Ligate Superior Thyroid artery as close to gland as possible due to its close approximation to External laryngeal nerve as it is away from gland. if Sup Thyroid is ligated away from gland, it may injure ELN Leading to Husky voice Ligate inferior thyroid artery as far away to gland as possible due to relation with recurrent laryngeal nerve. RLN injury may produce Hoarseness External Laryngeal nerve is injured most commonly in Thyroid surgeries RLN is commonly injured during tracheostomy
Parathyroid glands	<ul style="list-style-type: none"> 4 pinkish/ brown glands, Weighing 50mg & 6 x 3 x 2mm each Usually lie within pretracheal fascia Superior (develops from endoderm of Dorsal diverticulum of 4th pouch) is Less variation in position superior parathyroids are cranial to inf thyroid artery and posterior to RLN Inferior (dragged down with thymus from 3rd pouch) have More variation, even into upper mediastinum. Blood supply: Inferior thyroid arteries & Nerves: Sympathetic on arteries for Vasoconstriction Histology: Homogeneous , Very vascular Small round cells , No follicles , Irregular columns



TONGUE	<ul style="list-style-type: none"> Develops From occipital somite – the first somites to appear (Diaphragm from Cervical somites) all muscles of the tongue are Innervated by the hypoglossal nerve except palatoglossus Lingual artery is major blood supply of tongue , others: Tonsillar + Ascending pharyngeal artery Tongue Tie is best corrected at 3 to 4 yrs. od age All except the Filiform papillae have taste buds on their surfaces Filiform Papillae are smallest and the most numerous containing No taste buds Fungiform papilla are concentrated along margins of tongue and tip of tongue-mushroom shaped Circumvallate papillae are Largest, about 8 to 12 papillae in a single V-shaped line immediately anterior to the terminal sulcus Foliate papillae are linear folds of mucosa on sides of tongue near the terminal sulcus of tongue Salty taste detected by Anterior and lateral half of each side of tongue vie Na⁺ channels (ENaC) Sweet Taste caused by (sugar, Glucose, Alcohols, aldehydes, ketone) detected by Tip of tongue Umami taste (e.g., Burger / Pizza) uses Glutamate receptors . Proteins detected at the back of tongue mostly Bitter taste (alkaloid, quinine, caffeine, and nicotine) mediated by G- Protein and detected at posterior tongue (via glossopharyngeal nerve) Sour taste caused by acid, detected by lateral half of each side of tongue via Na channels (ENaC) Sweet, bitter & Umami taste use G-protein coupled receptor pathway. 						
Muscles	<ul style="list-style-type: none"> Intrinsic + Extrinsic muscles as given below; Intrinsic muscles originate and insert within substance of Tongue. They are divided into superior longitudinal, Inferior longitudinal, transverse, and Vertical muscles Extrinsic muscles There are 4 major extrinsic muscles on each side- Genioglossus, Hyoglossus, Styloglossus, and palatoglossus These muscles protrude, retract, depress, and elevate the Tongue. The Styloglossus muscles retract the tongue and pull the back of the tongue superiorly Hyoglossus muscle is an important landmark in the floor of oral cavity Genioglossus Protrudes anterior tongue out of oral fissure (stick the Tongue out) while depresses the central part of the tongue 						
Nerve supply	<table border="1"> <tr> <td data-bbox="336 1659 651 1760">Anterior 2/3rd tongue</td><td data-bbox="651 1659 1485 1760"> <ul style="list-style-type: none"> General sensation by Lingual nerve Taste sensation by Chorda tympani branch of facial nerve Chorda tympani carries Special visceral afferent -SVA </td></tr> <tr> <td data-bbox="336 1760 651 1798">Posterior 1/3rd</td><td data-bbox="651 1760 1485 1798"> <ul style="list-style-type: none"> Both general & taste sensation carried by Glossopharyngeal nerve. </td></tr> <tr> <td data-bbox="336 1798 651 1836">Posterior most</td><td data-bbox="651 1798 1485 1836"> <ul style="list-style-type: none"> Posterior most part of tongue is supplied by Vagus nerve </td></tr> </table> <p>Sympathetic supply of tongue is From Superior Cervical Ganglion via Lingual artery</p>	Anterior 2/3rd tongue	<ul style="list-style-type: none"> General sensation by Lingual nerve Taste sensation by Chorda tympani branch of facial nerve Chorda tympani carries Special visceral afferent -SVA 	Posterior 1/3rd	<ul style="list-style-type: none"> Both general & taste sensation carried by Glossopharyngeal nerve. 	Posterior most	<ul style="list-style-type: none"> Posterior most part of tongue is supplied by Vagus nerve
Anterior 2/3rd tongue	<ul style="list-style-type: none"> General sensation by Lingual nerve Taste sensation by Chorda tympani branch of facial nerve Chorda tympani carries Special visceral afferent -SVA 						
Posterior 1/3rd	<ul style="list-style-type: none"> Both general & taste sensation carried by Glossopharyngeal nerve. 						
Posterior most	<ul style="list-style-type: none"> Posterior most part of tongue is supplied by Vagus nerve 						
Lymphatics	<ul style="list-style-type: none"> Submental lymph node : Tip of tongue Submandibular lymph node : Anterior 2/3 and sides of tongue Jugulo-Omohyoid : Posterior 1/3rd of tongue All lymphatic vessels ultimately drain into deep cervical nodes along internal jugular vein 						



Tonsils	<ul style="list-style-type: none"> Palatine tonsils lined by Stratified Squamous epithelium and located in isthmus of the fauces between Palatoglossus and palatopharyngeous arches of soft palate Nasopharyngeal tonsils or Adenoids lined by Pseudo-stratified columnar epithelium Lingual tonsils lined by stratified squamous epithelium Waldeyer's ring is a circle of lymphoid tissue at upper end of GIT & respiratory tract, consists of 2 tubal tonsils, 2 palatine tonsils, 1 nasopharyngeal tonsil and 1 lingual tonsil as shown in diagram.
Palatine Tonsils	<ul style="list-style-type: none"> Lymphoid tissue in tonsillar fossa Anterior/posterior palatoglossal/palatopharyngeal arches , Superiorly - soft palate, Inferiorly- tongue Medial: mucosa + 20 tonsillar crypts, intratonsillar cleft (this is a large crypt from 2nd pharyngeal pouch) Tonsillar Bed: submucosa (capsule), superior constrictor, glossopharyngeal nerve , facial Artery & its branches Lymph to deep cervical & jugulodigastric nodes Veins: plexus in capsule to pharyngeal venous plexus. Also, External palatine V (Para tonsillar) from soft palate Nerves: tonsillar branch of glossopharyngeal (IX) - Referred pain to the middle ear. Lesser Palatine nerve also supplies some part (maxillary via pterygopalatine ganglion) Development: 2nd pharyngeal pouch endoderm gives Mucosa & crypts. Surrounding mesenchyme gives lymphoid tissue Surface marking: medial to lower masseter Most common Nerve to be injured in Tonsillectomy is : Glossopharyngeal nerve Vessel to be injured during tonsillectomy : External Palatine Vein > Ascending palatine/ascending Pharyngeal artery Read the stem of question carefully- if artery is being asked → Ascending palatine artery, a branch of facial Artery.



PHARYNX

- 5" (13cm) long fibromuscular tube suspended from skull lying anterior to prevertebral fascia
- **Extends from nose to C6 (oesophagus)** like a mask applied to back of face
- Walls are mucous membrane, fibrous submucosa, muscle and Thin buccopharyngeal fascia
- Muscles : 3 constrictors and longitudinal muscles (Stylopharyngeus, palatopharyngeus, salpingopharyngeus) and longitudinal muscles. Levator palatini is wholly intra-pharyngeal

Nasopharynx	<ul style="list-style-type: none"> • Extends from choanae to lower border of soft palate • On back and sides lies the pharyngobasilar fascia • posterior: prevertebral space or fascia, body of c1 vertebra • anterior: choanae & back of soft palate • epithelium: pseudo stratified ciliated columnar • Features: <ul style="list-style-type: none"> • opening of auditory tube, pharyngeal tonsil, tubal tonsil • pharyngeal recess of Rosen muller, salpingopharyngeus and levator palatini • Nerve supply: pharyngeal branch of maxillary nerve
Oropharynx	<ul style="list-style-type: none"> • Extends from lower border of soft palate to upper border of epiglottis • Anterior: posterior aspect of tongue & palatoglossal arch • Posterior: 3 constrictors & C2/C3 vertebrae • Inferior: back of tongue, lingual tonsil & valleculae • Lateral: palatoglossal/palatopharyngeal arches, constrictors, and palatine tonsil • Lining: squamous epithelium • Nerves: glossopharyngeal (IX) & internal laryngeal (X) • Features: Palatine tonsils, Lingual tonsils and Valleculae
Laryngopharynx	<ul style="list-style-type: none"> • Extends from: tip of epiglottis - C3 To start of oesophagus-C6 • Anterior: larynx, aditus, epiglottis • Posterior: 3 overlapping constrictors, dehiscence of Killian, cricopharyngeus, vertebrae C4,5,6 • Nerve supply: internal laryngeal nerve (X) & recurrent laryngeal nerve (X). • Lining: squamous non-keratinised epithelium • Features: aditus to larynx & piriform fossa

Clinical anatomy	Hypopharynx	<ul style="list-style-type: none"> ○ A clinical term for that part of the Laryngopharynx below the aditus ○ Anterior: arytenoid cartilages ○ Posterior: dehiscence of Killian ○ Killian's dehiscence is a gap between oblique and transverse fibres of inferior constrictor. A pharyngeal pouch (Zenker's diverticulum) can be formed by outpouching of pharyngeal mucosa at this site. ○ It is a common site for perforation during esophagoscopy, hence, called as Gateway of tear
	Piriform or smuggler's fossa	<ul style="list-style-type: none"> ○ Medial: quadrangular membrane ○ Lateral: thyrohyoid membrane & Lamina of thyroid cartilage ○ Supplied by internal laryngeal nerve ○ Bone impaction (e.g., fish bone) while eating commonly occurs here ○ Smugglers artificially deepen this fossa using lead balls to hide diamonds

STRUCTURES PASSING

Between skull base & superior constrictor	Eustachian tube, levator, and tensor palatini, ascending palatine artery
Between superior and middle constrictor	glossopharyngeal nerve & stylopharyngeus muscle
between middle and inferior constrictor	internal laryngeal nerve & superior laryngeal artery
below inferior constrictor	recurrent laryngeal nerve and inferior laryngeal artery

LARYNX

<ul style="list-style-type: none"> • Larynx is in front of C3-C4-C5-C6, while in infant it lies against the C2 - C3. • Benign tumors are less common than malignant tumors in the larynx. • Hoarseness is a prominent symptom of laryngeal cancer. • The highest incidence of distant metastases in laryngeal cancer is seen in Lung. • 6 Laryngeal cartilages: <ul style="list-style-type: none"> ○ 3 paired (Thyroid, cricoid, epiglottis), 3 unpaired (Arytenoid, cuneiform, corniculate) • Cricothyroidotomy is lifesaving, done through cricothyroid Membrane and requires no anaesthesia. • Tracheostomy is Ideal For temporary or permanent Intubation through 2nd & 3rd tracheal rings, usually after dividing thyroid Isthmus. It requires anaesthesia 		
Cartilages	Unpaired	<ol style="list-style-type: none"> 1. Cricoid cartilage: unpaired Signet ring like Complete circle, most inferior of laryngeal cartilage and completely encircles the airway , Inferior constrictor attached to it. Cricoid cartilage is derivative of 6th Branchial arch. 2. Thyroid cartilage : unpaired Shield like, Largest of laryngeal cartilage. The Adam's apple or laryngeal prominence is the protrusion formed by the angle of the thyroid cartilage surrounding the larynx. 3. Epiglottis: Elastic cartilage behind the root of tongue , Top & anterior surface is stratified Squamous epithelium. Posterior is Pseudostratified columnar. Held by hyo-epiglottic, thyro-epiglottic + aryepiglottic ligaments, median & lateral glosso-epiglottic folds
	Paired (ACC)	<ol style="list-style-type: none"> 1. Arytenoid: has a muscular + Vocal process. Cricoarytenoids + Cricothyroid joints are Synovial joints 2. Corniculate 3. Cuneiform
Laryngeal inlet	<ul style="list-style-type: none"> • It extends from tip of epiglottis to C6 and open for respiration. • partially closed for speaking while closed for coughing, straining, and swallowing • Hangs from hyoid bone via tongue/mandible (hyoglossus, mylohyoid Geniohyoid, digastric, middle constrictor) and by 3 of 4 strap muscles (omohyoid, sternohyoid & thyrohyoid) 	

	<ul style="list-style-type: none"> Inlet (or aditus) to larynx is made up of two Aryepiglottic folds, and it leads to vestibule. Larynx elevated by: Mylohyoid, digastric, stylohyoid, geniohyoid, thyrohyoid, stylopharyngeus, palatopharyngeus, Salpingopharyngeus, inferior constrictor 				
Vocal cords	<table> <tr> <td>True VCs</td><td> <p>They are the free upper edges of the cricothyroid membrane (conus elasticus) or cricovocal membrane where it is thickened to become the cricovocal ligament and covered with mucosa. The Mucosa is pearly white and has no submucosa and thus cannot become oedematous</p> <ul style="list-style-type: none"> 40% of the vocal cord is arytenoid cartilage while 60% is the membrane The cricothyroid membrane is attached around the inside of the ring of cricoid cartilage and has a free upper margin that is attached to the arytenoid cartilages posteriorly and to the back of the thyroid cartilage anteriorly Glottis refers to the vocal apparatus of the larynx, which consists of the true vocal folds (vocal cords) and the opening between the vocal cords, called the Rima glottides. Type of epithelium lining the vocal cords is non-keratinizing stratified Squamous. Phonation is produced by vibration of vocal cords </td></tr> <tr> <td>False VCs</td><td> <ul style="list-style-type: none"> Also called Vestibular folds, are the lowest edge of Quadrangular membrane Free edge of this membrane are aryepiglottic folds Pseudo stratified epithelium lines false Vocal cords Approximation of false vocal cords play imp role in deglutition process The opening between the false vocal folds is called Rima vestibuli or false glottis. </td></tr> </table>	True VCs	<p>They are the free upper edges of the cricothyroid membrane (conus elasticus) or cricovocal membrane where it is thickened to become the cricovocal ligament and covered with mucosa. The Mucosa is pearly white and has no submucosa and thus cannot become oedematous</p> <ul style="list-style-type: none"> 40% of the vocal cord is arytenoid cartilage while 60% is the membrane The cricothyroid membrane is attached around the inside of the ring of cricoid cartilage and has a free upper margin that is attached to the arytenoid cartilages posteriorly and to the back of the thyroid cartilage anteriorly Glottis refers to the vocal apparatus of the larynx, which consists of the true vocal folds (vocal cords) and the opening between the vocal cords, called the Rima glottides. Type of epithelium lining the vocal cords is non-keratinizing stratified Squamous. Phonation is produced by vibration of vocal cords 	False VCs	<ul style="list-style-type: none"> Also called Vestibular folds, are the lowest edge of Quadrangular membrane Free edge of this membrane are aryepiglottic folds Pseudo stratified epithelium lines false Vocal cords Approximation of false vocal cords play imp role in deglutition process The opening between the false vocal folds is called Rima vestibuli or false glottis.
True VCs	<p>They are the free upper edges of the cricothyroid membrane (conus elasticus) or cricovocal membrane where it is thickened to become the cricovocal ligament and covered with mucosa. The Mucosa is pearly white and has no submucosa and thus cannot become oedematous</p> <ul style="list-style-type: none"> 40% of the vocal cord is arytenoid cartilage while 60% is the membrane The cricothyroid membrane is attached around the inside of the ring of cricoid cartilage and has a free upper margin that is attached to the arytenoid cartilages posteriorly and to the back of the thyroid cartilage anteriorly Glottis refers to the vocal apparatus of the larynx, which consists of the true vocal folds (vocal cords) and the opening between the vocal cords, called the Rima glottides. Type of epithelium lining the vocal cords is non-keratinizing stratified Squamous. Phonation is produced by vibration of vocal cords 				
False VCs	<ul style="list-style-type: none"> Also called Vestibular folds, are the lowest edge of Quadrangular membrane Free edge of this membrane are aryepiglottic folds Pseudo stratified epithelium lines false Vocal cords Approximation of false vocal cords play imp role in deglutition process The opening between the false vocal folds is called Rima vestibuli or false glottis. 				
Muscles	<ul style="list-style-type: none"> Cricothyroid muscle is the tensor of vocal cord. Posterior cricoarytenoid is the only abductor of the vocal cord i.e Safety muscle of life Bilateral abductor paralysis is an emergency where both vocal cords are present in Para median Position and the patient has respiratory distress. To raise pitch or tone of voice: Cricothyroid is used ; To Lower tone or Pitch- Thyroarytenoid is used 				
Nerve supply of larynx	<table> <tr> <td>Motor</td><td> <ul style="list-style-type: none"> Superior laryngeal nerve (external branch) - Cricothyroid muscle All other muscles : Recurrent Laryngeal nerve </td></tr> <tr> <td>Sensory</td><td> <ul style="list-style-type: none"> Above the vocal cord : internal laryngeal nerve (passes between thyroid & hyoid bone) Below the vocal cord: recurrent laryngeal nerve </td></tr> </table> <ul style="list-style-type: none"> Superior laryngeal nerve a branch of vagus nerve divides into internal laryngeal nerve(sensory) and external laryngeal nerve (motor, closely related to superior thyroid artery). Recurrent laryngeal nerve a branch of vagus nerve is closely related to inferior thyroid artery and Supplies all the muscles of the larynx, except Cricothyroid, the mucus membrane of the larynx Below the vocal cord and the mucus membrane of the upper part of the trachea. The recurrent laryngeal nerves are the nerves of the sixth pharyngeal arch. Recurrent laryngeal nerve (RLN) injury results in true vocal-fold paresis or paralysis. 	Motor	<ul style="list-style-type: none"> Superior laryngeal nerve (external branch) - Cricothyroid muscle All other muscles : Recurrent Laryngeal nerve 	Sensory	<ul style="list-style-type: none"> Above the vocal cord : internal laryngeal nerve (passes between thyroid & hyoid bone) Below the vocal cord: recurrent laryngeal nerve
Motor	<ul style="list-style-type: none"> Superior laryngeal nerve (external branch) - Cricothyroid muscle All other muscles : Recurrent Laryngeal nerve 				
Sensory	<ul style="list-style-type: none"> Above the vocal cord : internal laryngeal nerve (passes between thyroid & hyoid bone) Below the vocal cord: recurrent laryngeal nerve 				

Vocal Cord Position	Associated Condition
Median	<ul style="list-style-type: none"> In the Midline. Normally occurs during Phonation.
Paramedian	<ul style="list-style-type: none"> 1.5 mm from Midline. Normally this position occurs during strong whispering Abnormally occurs during Isolated RLN Paralysis. Partial Adduction is Preserved from <ul style="list-style-type: none"> Cricothyroid (due to Intact SLN) interarytenoids (as it receives Bilateral Innervation)
Cadaveric (Intermediate)	<ul style="list-style-type: none"> 3.5 mm from Midline. Neutral position of Cricoarytenoid joint. Abduction and Adduction take place from this position. Abnormally occurs during complete Paralysis of both RLN and SLN
Gentle abduction	<ul style="list-style-type: none"> 7 mm from Midline. Normally occurs during Quiet Respiration
Full abduction	<ul style="list-style-type: none"> 9.5 mm from Midline. Normally occurs during Deep Respiration.

KEY FACTS

- Positions of Vocal Folds do not necessarily predict the site of lesion.
- Caused mainly by degree of Reinnervation and Synkinesis
- Unilateral or bilateral RLN paralysis → Median/paramedian Vocal cord- they do not abduct on deep inspiration.
- Unilateral RLN and superior laryngeal nerve Paralysis → Intermediate position, leads to glottic incompetence.
- Bilateral RLN and SLN paralysis → Intermediate position of vocal cord

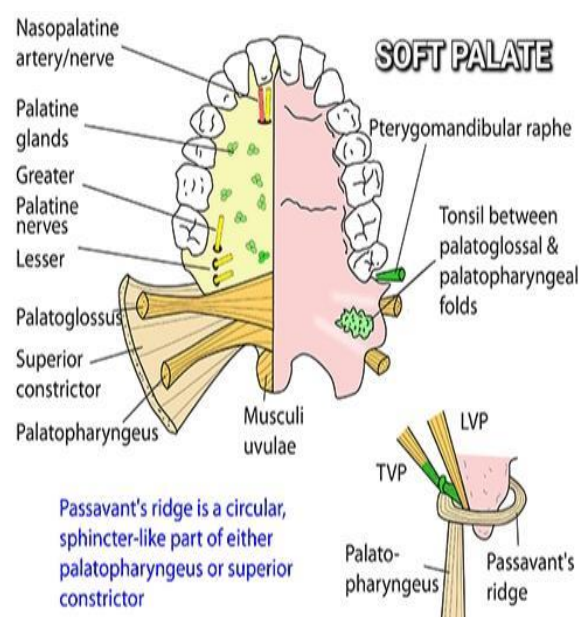
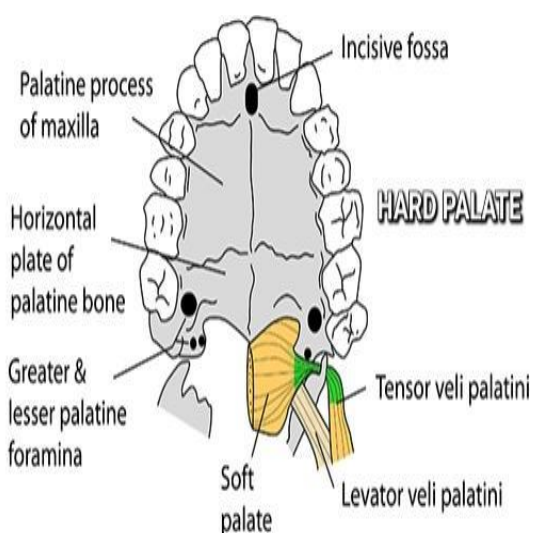
Condition of vocal cord	Muscle damaged	Muscle involved
Tense (RLN damaged)	Vocalis, Thyroarytenoid (prefer it)	Cricothyroid
Loose (ELN damaged)	Cricothyroid	Vocalis and Thyroarytenoid
Adducted	Posterior Cricoarytenoid is damaged	
Abducted	Lateral Cricoarytenoid is damaged	

SOFT PALATE

- Consists of aponeurosis and muscles
- Tensor veli palatini, Levator veli palatini, Palatoglossus, Palatopharyngeus and muscles of uvula, Mucosa, Mucous & serous glands, and, a few taste buds
- Epithelium: Stratified squamous non keratinized
- Blood supply: Lesser palatine artery (from maxillary artery), Ascending palatine artery (facial)
- Palatine branch of ascending Pharyngeal (external carotid)
- Veins: Pharyngeal & pterygoid plexus
- Lymph: Retropharyngeal & anterosuperior deep cervical Lymph nodes
- **Nerve supply:** Secretomotor fibres from maxillary nerve via Pterygopalatine ganglion
- Sensation via maxillary nerve and lesser palatine nerve (branch of CN IX)
- Taste sensations from palate carried by Greater petrosal & Lesser palatine nerves.
- Function of soft palate is to close the nasopharynx while swallowing

HARD PALATE

- Consists of Mucoperiosteum (mucosa + periosteum). Sharpey's fibres into pits on bone
- Blood supply: Greater palatine artery while Venous drainage: Pterygoid plexus
- Lymph: Retropharyngeal and deep cervical nodes
- Nerve supply: Greater palatine and nasopalatine nerves

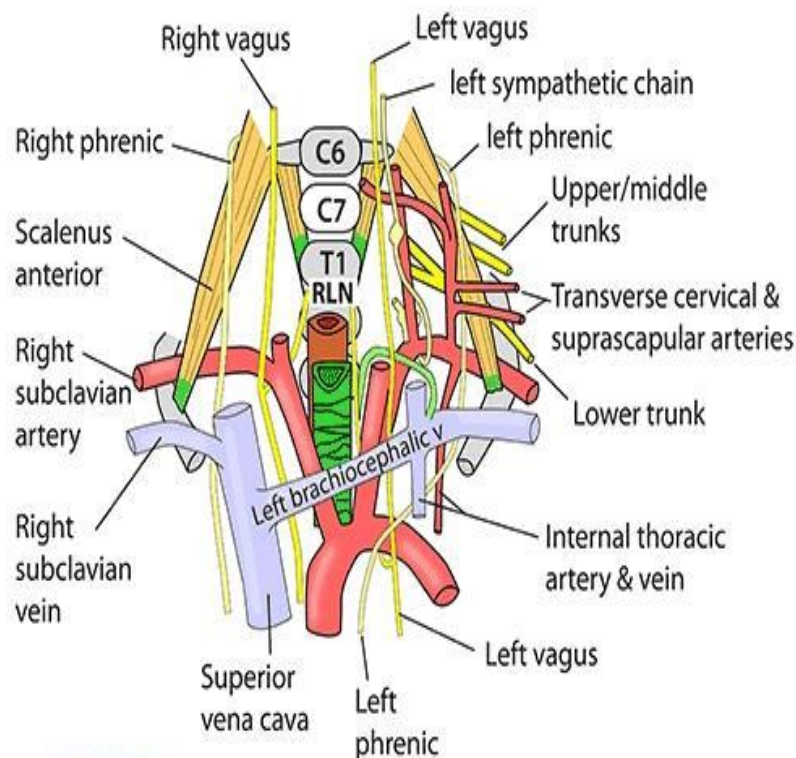


DEEP NECK SPACE	DESCRIPTION
Prevertebral space	<ul style="list-style-type: none"> ○ Closed space behind prevertebral fascia which allows infection to track down into axilla via the axillary sheath Which is also part of the prevertebral fascia. ○ When infection is post to prevertebral fascia or any other location(posterior to Pretracheal fascia or anterior to prevertebral fascia) then, it may spread to superior mediastinum ○ If infection is anterior to pretracheal fascia than it goes to anterior mediastinum.
Retropharyngeal space	<ul style="list-style-type: none"> ○ Situated Immediately anterior to prevertebral fascia. ○ Below, it extends behind oesophagus to diaphragm via superior & posterior mediastinum. ○ Infection may spread behind the carotid sheath into the posterior Triangle of neck
Parapharyngeal space	<ul style="list-style-type: none"> ○ It is the Lateral continuation of retropharyngeal space
Submandibular space	<ul style="list-style-type: none"> ○ Extends above investing layer of deep cervical fascia between hyoid and mandible to mucous membrane of floor of mouth. ○ Contains mylohyoid muscle, sublingual gland above this muscle and submandibular gland hooking around its Posterior border. ○ cellulitis may occur following dental procedures known as Ludwig's angina

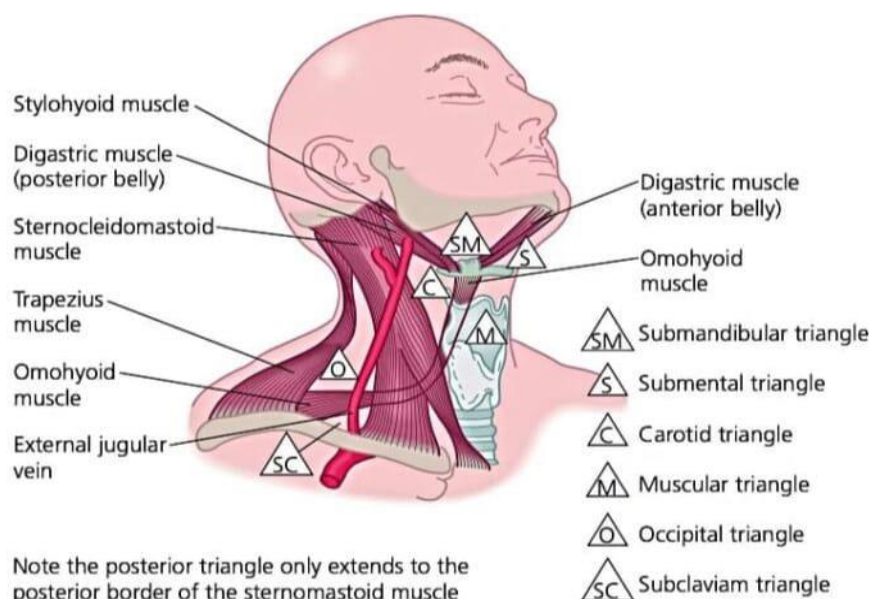
Important Relations of Scalenus anterior

Anterior	Phrenic nerve (under prevertebral fascia), carotid sheath., vagus nerve, thoracic duct
Posterior	2 nd part of subclavian artery, Costocervical trunk, scalenus Medius
Medial	Vertebral artery and vein . 1 st part of subclavian artery, thyrocervical trunk, stellate ganglion
Lateral	trunks of brachial plexus, 3 rd part of subclavian artery

RELATIONS TO SCALENUS ANTERIOR



TRIANGLES OF NECK											
Anterior Triangle	<ul style="list-style-type: none"> It consists of 4 triangles – submental, submandibular, carotid, and, muscular triangle. Submental is unpaired, while rest are paired ones. Boundaries <ul style="list-style-type: none"> Anteriorly – midline of neck Posteriorly – anterior border of sternocleidomastoid. Superiorly / base – by inferior border of mandible. Apex – by manubrium sterni. Contents: <table border="1"> <tr> <td>Muscles</td><td>Digastric, mylohyoid, superior belly of omohyoid, sternohyoid, strap muscles.</td></tr> <tr> <td>Vessels</td><td>External carotid artery and branches (except posterior auricular artery) Internal and anterior jugular vein</td></tr> <tr> <td>Nerve</td><td>Internal and external laryngeal nerves, nerve to mylohyoid, hypoglossal nerve</td></tr> <tr> <td>Viscera</td><td>Thyroid and larynx, submandibular and sublingual glands.</td></tr> <tr> <td>Others</td><td>Jugular lymph nodes.</td></tr> </table> 	Muscles	Digastric, mylohyoid, superior belly of omohyoid, sternohyoid, strap muscles.	Vessels	External carotid artery and branches (except posterior auricular artery) Internal and anterior jugular vein	Nerve	Internal and external laryngeal nerves, nerve to mylohyoid, hypoglossal nerve	Viscera	Thyroid and larynx, submandibular and sublingual glands.	Others	Jugular lymph nodes.
Muscles	Digastric, mylohyoid, superior belly of omohyoid, sternohyoid, strap muscles.										
Vessels	External carotid artery and branches (except posterior auricular artery) Internal and anterior jugular vein										
Nerve	Internal and external laryngeal nerves, nerve to mylohyoid, hypoglossal nerve										
Viscera	Thyroid and larynx, submandibular and sublingual glands.										
Others	Jugular lymph nodes.										
Submental triangle	<ul style="list-style-type: none"> Apex – formed by symphysis of mandible, while Base – formed by hyoid bone. Floor – by mylohyoid muscles. laterally demarcated by anterior bellies of digastric. It contains lymph nodes and the small veins that drain into anterior jugular vein. 										
Submandibular or Digastric triangle	<ul style="list-style-type: none"> Anteriorly formed by ant bely of digastric, while posteriorly by posterior belly of digastric. Superiorly – lower border of mandible body Floor is formed anteriorly by mylohyoid, while posteriorly by hyoglossus muscle. Contents <ul style="list-style-type: none"> marginal mandibular nerve, submandibular gland – which has facial vein superficial to it and facial artery deep to it. Lower part of parotid gland in posterior part. 										
Carotid triangle	<ul style="list-style-type: none"> It is bounded: <ul style="list-style-type: none"> Superiorly – by posterior belly of diagastric. Laterally – by posterior border of SCM. Medially – by superior belly of omohyoid. Floor – by thyrohyoid, hyoglossus muscles, inferior & middle pharyngeal constrictors. Contents: <ul style="list-style-type: none"> Arteries – common carotid, with its division into ECA & ICA. Nerves – vagus , hypoglossal nerve, superior root of ansa cervicalis. Superior laryngeal N. 										
Muscular triangle	<ul style="list-style-type: none"> Anteriorly – bounded by midline from hyoid bone to sternum. Inferolaterally – anterior border of SCM. Superolaterally – superior belly of omohyoid. Contents: strap muscles and parathyroid glands. 										



Occipital triangle + Subclavian triangle } Posterior triangle

Submental triangle + Submandibular triangle + Carotid triangle + Muscular triangle } Anterior triangle

Triangles of the neck



Posterior triangle	It is divided into suboccipital and subclavian triangles by inferior belly of omohyoid.
Occipital triangle	<ul style="list-style-type: none"> Upper and bigger part of posterior triangle. It is bounded: Anteriorly – posterior border of SCM. Posteriorly – ant border of trapezius. Inferiorly – inferior belly of omohyoid. Floor formed by splenius capitis, levator scapulae, and, scalene muscles. Contents: <ul style="list-style-type: none"> Spinal accessory nerve / CN XI, supraclavicular nerve, branches of cervical plexus and upper most part of brachial plexus,
Subclavian triangle	<ul style="list-style-type: none"> Lower and smaller part of posterior triangle. Boundaries: <ul style="list-style-type: none"> inferior belly of omohyoid, clavicles and posterior border of SCM. It contains --- third part of subclavian artery, first rib, brachial plexus, supraclavicular nerves, scalenus medius, domes of pleura

EYE

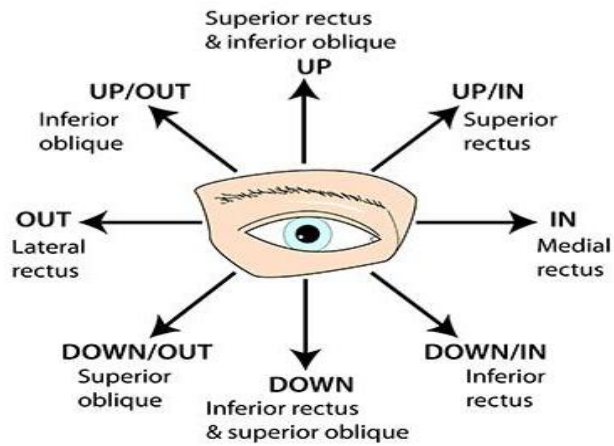
Tenon's capsule	<ul style="list-style-type: none"> Fascial sheath of eye, bursa behind the eyeball. Inner layer blends with sclera Outer layer pierced by tendons and also extends back along them There is not normally any posterior displacement of the eyeball due to; Medial/lateral check ligaments, Presence of orbital fat and forward pull of 2 oblique muscles 												
Orbital septum	<ul style="list-style-type: none"> Anterior lacrimal crest and margins of orbit Tarsal plates are the fibrous thickening of orbital septum Meibomian glands: present in tarsal plate- modified sebaceous glands secreting oil Blood supply of lids by palpebral branches of ophthalmic artery Nerves: Upper skin/conjunctiva supplied by lacrimal, Supra-orbital, Supra-& infratrochlear nerves Lower skin/conjunctiva via infra-orbital nerve Levator palpebrae superioris Arises from bone above tendinous ring and insert at Eyelid, tarsal plate & Conjunctival sac Nerve supply:(oculomotor) to all three insertions (somatic) so defect gives complete ptosis Sympathetic to tarsal plate only (autonomic) : so, this defect gives Only partial ptosis For the muscle to function correctly both somatic and Sympathetic supply must be intact 												
Lacrimal gland	<ul style="list-style-type: none"> Serous gland in lacrimal fossa (lateral roof of orbit) via 10-12 ducts draining into lateral or superior fornix of conjunctiva. Tears swept medially by progressive lid closure Histology shows stratified epithelium containing serous acini Nerve supply: Secretomotor fibres from Superior salivary nucleus to Facial nerve → greater petrosal nerve to pterygopalatine ganglion → zygomatic branch of maxillary Division of trigeminal (V2) to zygomaticotemporal nerve to connecting branch in orbit to lacrimal nerve (V1) → Gland Blinking achieved by palpebral part of orbicularis oculi (no tear Spill) Screwing up achieved by orbital part of orbicularis oculi (tear Spill and squeezes lacrimal sac) Lacrimal sac lies between anterior & posterior lacrimal crests with palpebral fibres of orbicularis oculi inserting into its walls to draw it open and suck in tears Nasolacrimal duct is 2cm long, drains into inferior meatus of Lateral wall of nose & its mucosal folds are valvular (Haser's valve) to stop air ascending. 												
Layers of eyeball	<ol style="list-style-type: none"> Outer layer : The sclera and cornea make up the exterior layers. The uvea is the vascular layer in the middle, subdivided into the iris, ciliary body, and choroid. The retina constitutes the innermost layer and is made up of nervous tissue. 												
Extraocular muscles & movements	<table border="1"> <tbody> <tr> <td>Medial rectus</td><td>Moves the eye Medially</td></tr> <tr> <td>Lateral rectus</td><td>Moves the eye Laterally</td></tr> <tr> <td>Superior rectus</td><td>Moves the eye Upward & Medially</td></tr> <tr> <td>Inferior rectus</td><td>Moves the eye inferiorly & medially</td></tr> <tr> <td>Superior oblique</td><td>downward + outward/lateral movement of eye (Inferolateral) intorsion of eye</td></tr> <tr> <td>Inferior oblique</td><td>Upward + outward/lateral movement of eye (Superolateral) - extorsion of Eye</td></tr> </tbody> </table> <p><u>TORSION OF EYEBALL</u></p> <ul style="list-style-type: none"> Because of the oblique angle of the orbit and the way that the muscles Attach distal to the equator of the eye there is a tendency for some of the muscles to twist the eye in addition to its main action. This torsion, which can be internal (intorsion) or external (extorsion), is important as it counteracts the tilting movements of the head. The degree of twisting for any one muscle is determined by whether the eyeball is abducted or Adducted The action of superior oblique is to pull its attachment to the globe Upwards and medially. This will turn the cornea/eye downwards and outwards. Similarly, the inferior oblique does the opposite, turning the Cornea/eye upwards and outwards. We know that the isolated action of superior oblique is to turn the eye downwards & outwards. But lateral rectus & inferior rectus, acting Together, could achieve the same action. By asking the patient to first Look inwards (to negate the action of lateral rectus) & 	Medial rectus	Moves the eye Medially	Lateral rectus	Moves the eye Laterally	Superior rectus	Moves the eye Upward & Medially	Inferior rectus	Moves the eye inferiorly & medially	Superior oblique	downward + outward/lateral movement of eye (Inferolateral) intorsion of eye	Inferior oblique	Upward + outward/lateral movement of eye (Superolateral) - extorsion of Eye
Medial rectus	Moves the eye Medially												
Lateral rectus	Moves the eye Laterally												
Superior rectus	Moves the eye Upward & Medially												
Inferior rectus	Moves the eye inferiorly & medially												
Superior oblique	downward + outward/lateral movement of eye (Inferolateral) intorsion of eye												
Inferior oblique	Upward + outward/lateral movement of eye (Superolateral) - extorsion of Eye												

	then downwards (inferior rectus is largely disabled when the eye is turned in) we test the Isolated downward action of superior oblique
Nerves	<ul style="list-style-type: none"> • All extraocular muscles are supplied by oculomotor nerve (CN III) except • superior oblique by trochlear nerve (CN IV) and lateral rectus by abducent nerve (CN VI) • Mnemonics = SO4 , L46 , rest all 3
OPTIC NERVE (SSA)	<ul style="list-style-type: none"> • Optic nerve is SSA or Special Somatic afferent. Optic nerve axon arise from the nerve cells of the ganglionic layer of retina and it units with the Opposite nerve of the opposite side to form the Optic Chiasma • in optic Chiasma, fibre from Medial (nasal) half of each retina cross the midline and enter the optic tract of the opposite side. Whereas the fibre from the lateral (temporal) half of each retina pass posteriorly in the optic tract of the same side. Most of the fibre of optic tract terminate by synapsing with nerve cell in lateral Geniculate body-few fibres pass to the Pretectal nucleus and superior colliculus of the midbrain, • However, and concerned with light reflex , the axon of the nerve cells of the lateral Geniculate Body pass posteriorly as the optic radiation and terminate in the visual cortex of the cerebral Hemisphere. • The paraventricular pathway from lateral geniculate nucleus to visual cortex is most Sensitive for color contrast
OCULOMOTOR NERVE	<ul style="list-style-type: none"> • 3rd cranial nerve , a motor nerve originating from midbrain and appears interpeduncular fossa • All extraocular muscles with the exception of lateral rectus (supplied by 6th cranial nerve) and superior oblique (supplied by 4th cranial nerve). • The GSE fibres Originate from the somatic component of oculomotor nucleus (also termed the somatic motor Nucleus). • General visceral efferent fibres: They originate from the parasympathetic component of Oculomotor nucleus (also termed the Edinger Westphal nucleus). They supply the sphincter Pupillae and ciliaris muscles. All these relay in the ciliary ganglion and are preganglionic Parasympathetic fibres. The postganglionic parasympathetic fibres supply the sphincter pupillae & ciliaris muscles and originate from the ganglion. • The oculomotor nerve originates from the anterior of the midbrain and appears in the Interpeduncular fossa. The nerve then travel forwards, below the posterior cerebral artery and above the superior Cerebellar artery, before piercing the dura mater and entering the cavernous sinus. • Within the cavernous sinus, the oculomotor nerve is located uppermost, above the trochlear Nerve in the lateral wall of the sinus, it enters the orbit via the superior orbital fissure as two branches: superior division and inferior Division • The superior division, the smaller of the two, runs above the optic nerve and gives branches to superior rectus and levator palpebrae superioris muscles which it supplies with motor fibres. • The inferior division supplies the inferior rectus, medial rectus (this branch passes below the optic Nerve), and the inferior oblique. It also gives off the parasympathetic root to the ciliary ganglion. • Accommodation is and action of Oculomotor nerve, by contraction of ciliary muscle • Damage to Edinger Westphal nucleus result in loss of papillary light reflex because Preganglionic fibre for constrictor papillae lies in Edinger Westphal nucleus
Optic Nerve lesions	<ul style="list-style-type: none"> • Lesion of the optic nerve causes blindness in the ipsilateral eye • Lesion of the Central or (middle) part of optic chiasm (often result of pituitary tumor or Meningioma) causes heteronymous Bitemporal hemianopia • Bitemporal hemianopia is seen with aneurysm of circle of Willis • Lesion of the optic tract causes homonymous contralateral hemianopia • Occlusion of the posterior cerebral artery results in homonymous hemianopia of the Contralateral visual field with macular sparing • Lesion of the geniculocalcarine tract causes homonymous hemianopia with macular sparing • Trick To Remember • Homonymous hemianopia in Question will be converted into optic tract and the left of the question will be converted into Right.

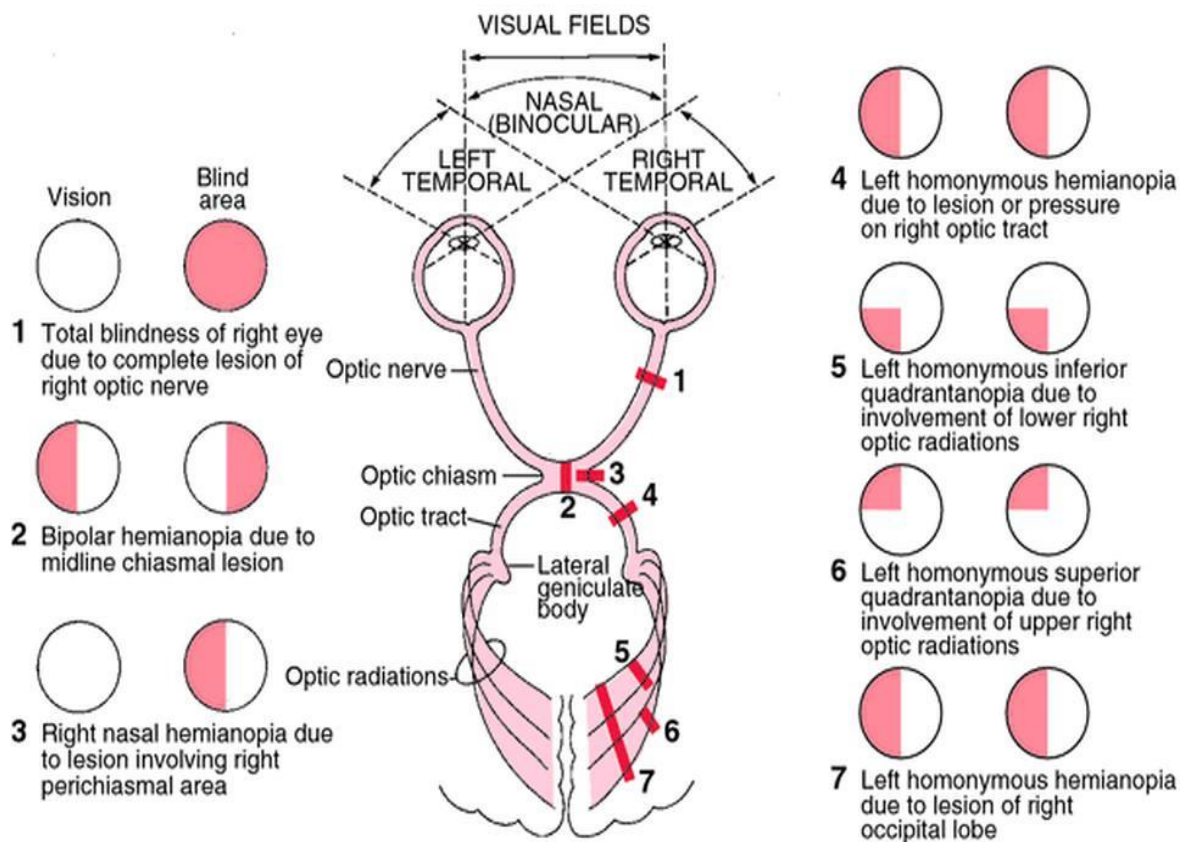
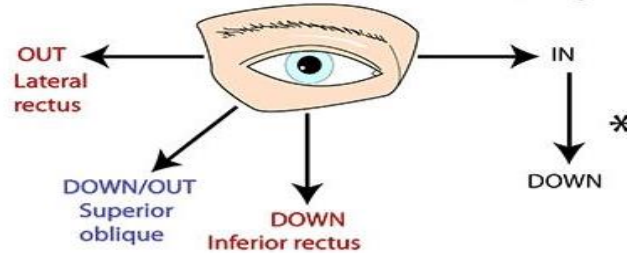
	<ul style="list-style-type: none"> • Contralateral heteronomous hemianopia for Optic chiasma lesion • Contralateral Homonymous hemianopia for Optic tract or Optic radiations lesions • If injury at Occipital region with homonymous hemianopia → Optic Radiations > Optic tract lesion • Macula is spared in Geniculocalcarine tract lesion
Oculomotor nerve lesions	<ul style="list-style-type: none"> • Ptosis: Ptosis with dilated pupil : Oculomotor nerve palsy Ptosis with constricted pupil : Horner syndrome Ptosis with normal pupil : Myasthenia gravis • Horner's Syndrome due to lesion of Sympathetic Ganglion (e.g., Superior Cervical ganglion). Features are; Ipsilateral Ptosis – drooping of eyelid , Ptosis is the most prominent sign. Ipsilateral Miosis – pupil constriction and Anhydrosis or Loss of Sweating on effected side • Remember that; Permanent Ptosis occurs at lesion of T4 > C3/C4
Diplopia	<ul style="list-style-type: none"> • Isolated Sixth cranial nerve palsy causes Horizontal Diplopia. • Isolated fourth cranial nerve palsy causes vertical diplopia. • Third cranial nerve palsy leads to both horizontal and vertical diplopia • diplopia on coming downstairs is called vertical diplopia- present both in 4th and 3rd Nerve palsy but CN 4 > CN 3 • All horizontal movements of eye are disturbed in lesion of pons . • All vertical movements of eye are disturbed in lesion of Midbrain.
Strabismus	<ul style="list-style-type: none"> • Misalignment of Eyes or squint. Following are the types ❖ Esotropia or convergent squint – inward turned eyes ❖ Exotropia or divergent squint – outward turned eyes ❖ Hypertropia or vertically displaced upward eyes ❖ hypotropia or vertically displaced downwards eyes ❖ Exophoria and esophoria is the turning of the eye outward and inward respectively from the active position when fusion is suspended ○ cover test is used to detect and confirm tropias ○ uncover test is used to detect and confirm phorias (latent squint) ○ alternate cover test or cross over test is used to detect total deviation= both phorias and tropias. ○ amblyopia or lazy eye is the feared complication of Squint – can lead to blindness
Key Facts	<ul style="list-style-type: none"> • Optic groove develops on left side of forebrain on day 22 • Retina develops from Optic vesicle • Ciliary body develops from Neuroectoderm & Mesoderm • Ciliary epithelium : from Neuroectoderm • Epithelium of Cornea : St. Squamous Non keratinized • Epithelium of Conjunctiva : Str Columnar epithelium • Visual cortex. Is the site of fusion of Binuclear vision • Pretectum – centre for Light reflex • Corneal reflex → Afferents : CN V , Efferents : CN VII • Visual pigment of Rods is rhodopsin = opsin + 11-cis Retinal • Basic Mech in Aqueous humor production is Active sodium secretion • Power of Eye is 59 Dioptres. Main factor is Anterior surface of Cornea > Lens • In children with lacrimal duct obstruction, Messaging with Observation is effective in 90% cases • Probing need to be delayed till 12-18months • Optic nerve arises from Ganglion cell layer of retina • There are 10 layers of retina. Rods & cons are in 4th layer • Magnocellular pathway (layer 1,2) carries information about form, movement, depth, and differences in brightness. So, it a Color-blind pathway • Parvocellular pathway carries information on color and fine detail. (layers 3,4,5,6) • The optic chiasma allows us to coordinate information between both eyes and is produced by crossing optical information across the brain.

Clinical pearls

- **Protanopia** : red cones defective- can't differentiate red from green
- **Duetranopia**- green cones are defective- can't differentiate green from red or blue
- **Tritanopia**: blue cones cells are defective
- **Remember it like** → really gone blind -- **RGB** = RED , GREEN , BLUE
- **Pituitary Adenoma**
 - If anteriorly grows, it may compress optic nerve
 - if grows superiorly, it can compress central or middle part of optic chiasma
 - If grows laterally, it may compress cavernous sinus
 - If grown inferiorly, it may affect sphenoid sinuses
- **Corneal Ulcers**
 - Dendritic/ Branching ulcer is seen in Herpes simplex keratitis- use Acyclovir
 - Bacterial ulcer presents acutely (1-2 wks.) , organisms involved: S.Pneumoniae , H.influenza , S aureus
 - Fungal ulcer presents within 3-4 wks. History of Injury with wooden stick in farmers especially
- **Hyphaema** : Blood in anterior chamber of eye
- **Anterior Uveitis** : Diagnosed by cells in anterior chamber
- **Retinal Detachment** : 4Fs = Floaters , Flashes , field loss (visual) , falling visual acuity
- **Cataract** : Glare is present, Gradual painless vision loss. causes are aging , Steroids , DM , UV light.
 - Phacoemulsification with IOL placement is gold standard therapy.
 - Snowflake pattern of cataract seen in diabetes.
 - Sunflower or rosette pattern cataract seen in Traumatic cataract.
- **Glaucoma** May be open or closed angled.
 - Optic disc cupping is seen in Angle closure glaucoma with byonetting sign.
 - Use beta blockers as 1st line agent in angle closure type.
- **Complications Of Diabetic Retinopathy:**
 - Neovascularization or 100 days glaucoma. Vitreous haemorrhage and Retinal detachment
 - Earliest feature of diabetic retinopathy is Microaneurysm.
 - Soft exudates are Micro infarcts while Hard exudates consist of Lipid cholesterol and proteins.
- **Hypertensive Retinopathy**
 - AV nipping , AV crossing signs , steple sign , constriction of vessels
 - Soft exudates and hard exudates seen. Macular star present in stage 4
- **Retinoblastoma** Associated with RB gene (autosomal dominant pattern).
 - Most commonly spreads by Optic nerve. Leucocoria or white reflex is present in it.
- **Central Retinal Vein Occlusion (CRVO)**
 - Tomato Splash or Blood and thunder appearance of fundus with cattle truck formation.
 - Sudden painless vision loss in a DM > HTN patient
- **Central Retinal Artery Occlusion (CRAO)**
 - Cherry red spot in macula is seen. Sudden painless vision loss in diabetic or HTN patient
- **Trachoma** is the most common infectious cause of blindness Worldwide (overall is Cataract)
- Follicles are seen in conjunctiva. prophylaxis with Erythromycin ointments
- **Trichiasis**: Inward grown eye lashes
- **Retinitis Pigmentosa** : autosomal dominant disease , bony spicules are seen in fundus with retinal atrophy.
- **Spring Or Vernal Conjunctivitis** : itching , photophobia , foreign body sensation in eye , mucoid discharge, rope like feeling in eyes. treat with anti allergics , steroids and mast cell stabilizers
- **Macular Degeneration** : Blurry or fuzzy vision. Difficulty recognizing familiar faces. Straight lines appear wavy. A dark, empty area or blind spot appears in the centre of vision. Loss of central vision, which is necessary for driving, reading, recognizing faces and performing close-up work.



TESTING ACTION OF SUPERIOR OBLIQUE



EAR

- Anatomically, ear has 3 parts → External , Middle , Inner ear.
- Inner Ear reaches adult size at Infant / childhood stage.

External ear	<p>Has following parts :</p> <ul style="list-style-type: none"> • Pinna: Amplification + Localisation of sound, has Elastic cartilage • External Auditory meatus: 3cm long, 2/3rd bone, 1/3rd cartilage, curves forwards Hairs and Glands (Sebaceous + Ceruminous) are present • Outer eardrum • Blood supply: Posterior auricular, Superficial temporal, Deep auricular (maxillary) artery • Lymph nodes: Pre-auricular, Mastoid and Superficial cervical nodes • External meatus/drum is Supplied by Auriculotemporal nerve with facial branch via Tympanic plexus • Greater auricular nerve supplies ear lobule and Lesser occipital on posterior side of auricle • Ramsay- Hunt syndrome: triad of Ipsilateral facial palsy, Otagia and Vesicles in outer ear canal caused by varicella zoster virus-the same virus for chickenpox • Perichondritis of Pinna: Pseudomonas is the common cause • Boxer's Ear/Cauliflower Ear : seen in boxers, during fight damage to the pinna leads to blood accumulation inside pinna forming hematoma and later cauliflower like appearance. Treated with Aspiration.
Middle ear	<ul style="list-style-type: none"> • A small air-filled cavity in the petrous part of the temporal bone • It contains Ossicles, Facial nerve, Chorda tympani, Inner eardrum, Auditory tube • Concentration of normal air in the middle ear: Nitrogen: 83%, oxygen: 9%, carbon dioxide 6% • The middle ear Transfers & enhances vibrations of the tympanic membrane by means of the ossicles - malleus, incus, and stapes. The signal is then passed via the foot plate of the stapes in the oval window to the labyrinth of the inner ear. • Auditory Tube : Opens on swallowing to equalise pressure, 3.5cm long, 1/3rd bone, 2/3rd cartilage, 30 degrees downwards, 45 degrees ant/med, Tubal tonsil at exit in Nasopharynx, Mucosa valve like Sensory supply via (maxillary nerve) and IX nerve <p><u>Walls Of Middle Ear (06)</u></p> <p>Middle ear is a six-sided slit like cavity like a "Match box"</p> <p>Superior wall or Roof: A thin plate of bone called the Tegmen tympani forms the roof, it Separates the tympanic cavity from middle cranial fossa</p> <p>Inferior wall or floor : Thin plate of bone which separate tympanic cavity from the Jugular Bulb</p> <p>Anterior wall: Thin plate of bone which separate the tympanic cavity from internal carotid Artery, and having two opening the upper one is for the canal of tensor tympani muscle and Lower one is for the Eustachian tube.</p> <p>Posterior wall: Aditus to the mastoid antrum below this is a hollow, conical projection From whose apex emerge the tendon of Stapedius muscle</p> <p>Lateral wall: Tympanic membrane</p> <p>Medial wall: The lateral of the inner ear and is formed by the labyrinth</p> <p>It Contains:</p> <ul style="list-style-type: none"> • Promontory: Rounded projection resulting from the underlying first coil of the cochlea • Oval window or the fenestra vestibule: Covered by the footplate of stapes. • Round window or the fenestra cochlea: covered by secondary tympanic membrane • Facial canal: Above the oval window is the canal for facial nerve. <p><u>Contents & Connections of Middle Ear</u></p> <ul style="list-style-type: none"> • 3 ossicles (malleus, incus, stapes) are of almost adult size at birth, inc the amplitude of vibration about 15-20 times due to leverage action & ear drum to oval window ratio. synovial joints are present in bones. Ear bones are irregular type of bones. Stapes is the shortest bone in the body. • Contains air, Auditory tube & Connects via an aditus posteriorly to the mastoid air sinus • Middle ear connects to the nasopharynx via the auditory tube for access of air & to keep the air Pressure equilibrated by opening with each swallow

- Contains two small muscles: tensor tympani & stapedius, which attach to Malleus and stapes respectively that dampen movements of these ossicles to avoid over-vibration during low pitched sounds.
- Has the facial nerve passing through it from the internal acoustic meatus to the Stylomastoid foramen. It is joined by Nervus intermedius, carrying general sensory, Taste & parasympathetic fibres, at the geniculate ganglion. Greater petrosal nerve leaves at this ganglion to pass eventually to the pterygopalatine ganglion.
- Facial Nerve gives a small motor branch to stapedius and then the chorda tympani Leaves it just before it exits the middle ear. The chorda tympani passes back into the Middle ear, crosses the pars flaccida of the tympanic membrane then exits forwards. From the middle ear finally to join the lingual nerve
- Has a tympanic branch of the glossopharyngeal nerve (IX) supplying sensation to it. it also supplies parasympathetic to the parotid gland via the lesser petrosal nerve and otic ganglion.
- Middle ear has a sensory supply largely from glossopharyngeal (IX) with a small contribution from facial
- blood supply from tympanic branch of maxillary & Stylomastoid branch of Posterior auricular artery.
- May fill with fluid or pus when infected & transmission of sound via the ossicles is Less efficient than sound passing directly through the bone. This is tested with a Tuning fork.

Tympanic membrane

- Derivative of all 3 layers but mostly (Ectoderm + Endoderm)
- Has 2 parts: Pars Tensa + Pars Flaccida
- Vibrates with incoming sound. Needs equal air pressure on Each side of it.
- It has 3 layers : Inner- low columnar (endodermal layer), Middle-fibrous and Outer Str. Squamous ectodermal layer)
- 1cm diameter, Pearly grey & shiny, 55 degrees to horizontal and concave outwards
- Faces downwards, forwards & laterally. Pulled inwards by tensor tympani
- Sensory supply
- Inner – glossopharyngeal (IX) and Outer – auriculotemporal nerve
- **Cone of Light** : Antero-inferior Quadrant of TM

Auditory tube

- Develops from 1st pharyngeal pouch, 3-3.5cm long 30 degrees downwards,
- 45 degrees anteromedially, 1/3rd bone + 2/3rd cartilage
- Blood supply from ascending pharyngeal & middle meningeal artery
- Tubal tonsil at exit in nasopharynx
- Auditory tube Opens on swallowing to equalise pressure, Mucosa is valve like
- Sensation via pharyngeal branch of maxillary nerve in lower part and glossopharyngeal (IX) in upper part (hence referred pain to middle ear from tonsils and oropharynx)
- Bony part in petrous temporal bone has columnar epithelium and Cartilaginous part in squamotympanic fissure has ciliated columnar epithelium
- Muscles opening it are: Salpingopharyngeus, Levator veli palatini and Tensor veli palatini

Glue Ear /Acute Serous Otitis Media : Infection of middle ear mostly in school going children.

Symptoms include decreased hearing , delayed speech.

Treat with Ear toilet , antibiotic, and decongestants. Myringotomy with grommet insertion is an effective therapy.

Inner ear

- Found in petrous part of temporal bone. Inner ear has bony and membranous labyrinth
- **Bony labyrinth** contains perilymph, semi-circular canals, vestibule, and cochlea
- **Membranous labyrinth** has sacs and ducts suspended in bony labyrinth
- 1. cochlear duct (scala media)
- 2. utricle & saccule → their maculae detect linear acceleration
 - utricle detects horizontal acceleration e.g., travelling in vehicle
 - saccule detects vertical acceleration e.g., while going up in elevator / lift
- mnemonics = Uhsv → utricle horizontal and saccule vertical.
- 3. Semi-circular ducts → ampullary crests detect rotational movement of head
 - Example : while doing cartwheel semi-circular canal of same side is activated to detect acceleration.
- **Parts of cochlea** → scala tympani , scala media and scala vestibuli
 - Scala media contains the **endolymph** (endolymph has more K⁺, potential of 80mv , resembles ICF)
 - Perilymph** : resembles ECF , has more Na⁺, potential of 0 mv , present in scala tympani & scala vestibuli

Hearing loss	<ol style="list-style-type: none"> Conductive hearing loss: Rinne's test +ve (abnormal) :bone Conduction > air conduction Weber test: localized to affected ear Sensorineural hearing loss: Rinne's test: Normal : air conduction > bone conduction Weber test: localized to unaffected ear <p>Noise-Induced: Damage to stereociliated organ of Corti- loss of high frequency hearing First Sudden extremely loud noises can produce loss due tympanic membrane rupture. Hearing loss in a person constantly exposed to loud noises e.g., jet loud noise is due to sensory neural hearing loss</p>
Key Facts	<p>TYMPANIC REFLEX: The tympanic reflex helps prevent damage to the inner ear by dampening Transmission of vibrations from the tympanic membrane to the oval window. The reflex has a Response time of 40 milliseconds, not fast enough to protect the ear from sudden loud noises Such as an explosion or gunshot</p> <ul style="list-style-type: none"> • Ear ossicles are almost of adult size at birth • Human can hear best in frequency range of 1000-2000db • Endolymph contain high potassium, also remember that tear has the highest Concentration of Na' • Nystagmus is caused by endolymph in semi-circular canal • Benign paroxysmal positional vertigo(BPPV): Dix-Hallpike/Barany manoeuvre along with typical Patient history-diagnostic for BPPV • Alternobaric vertigo: Failure to equalize pressure of the inner ear on ascent • In parotid gland swelling with no lymphadenopathy- Fine needle aspiration is done (FNAC) • Parotid swelling with otorrhea and lymphadenopathy → do Trucut biopsy • Otosclerosis is Spongy bone defect <p>Paracusis willisii: This occurs in otosclerotic patient who hears better in noisy environment than in quiet Surrounding because normal person will raise his voice in noisy surrounding. Stapedectomy / Stapedotomy with Prosthesis placement is the treatment of choice.</p> <p>Cholesteatoma: Skin in the ear or skin in the wrong place behind ear drum. A skin lined cyst that begins at the margin of the eardrum and invades the middle ear and mastoid.</p> <p>Chronic Suppurative Otitis Media: Chronic > 03 months infection of middle ear cleft with Ear Discharge and persistent perforation of tympanic membrane leading to reduced hearing</p> <p>2 TYPES:</p> <ul style="list-style-type: none"> • Tubotympanic Type (Mucosal disease): Safe type with Central TM perforation and involved antero-inf part of middle ear cleft i.e., eustachian tube + Mesotympanum • Atticoantral Type (Squamous disease): Unsafe type with Attic or Marginal perforation, involves postero-superior part of middle ear cleft i.e., attic, antrum and mastoid. It is associated with Cholesteatoma and serious complications e.g., Meningitis, Brain Abscess /Cavernous sinus thrombosis and Facial Palsy <p>REFERRED PAIN</p> <ul style="list-style-type: none"> • Pain in acute tonsillitis is referred to the ear through 9th nerve • Also Remember the nerve damage in tonsillectomy is 9th nerve • Pain in cancer larynx is referred to the ear through 10th nerve • Pain in cancer of pyriform fossa is referred to ipsilateral ear via 10th nerve • Pain in Temporo-mandibular Joint is referred to the ear through 5th nerve • Pain in salivary calculus referred to the ear through 5th nerve • Pain in acute sinusitis is referred to the ear through 5th nerve • Also, remember that Pain in Parotitis is due to stretching of tough fibrous capsule while pain is Transmitted via Auriculotemporal nerve caused by compression of the nerve • Pain of mumps is carried by greater auricular nerve - not auriculotemporal nerve <p>Controversial BCQs</p> <ul style="list-style-type: none"> • Read the stem carefully if Nerve is asked or cause being asked. <ol style="list-style-type: none"> 1. Pain of parotid gland or parotid region is carried by Greater auricular nerve 2. Pain of Parotitis is caused by Compression of : Auriculotemporal nerve 3. Pain of Parotitis or parotid gland is due to : Stretch or Tightening of Capsule of Parotid

NOSE

- Frontonasal Prominences give rise to Forehead, bridge of nose, medial and lateral nasal Prominence
- Maxillary prominence gives rise to Cheeks and lateral portion of upper lip
- Medial Nasal prominence → Philtrum of upper lip crest and tip of nose
- Lateral Nasal Prominence → Ala of nose and lateral nasal wall
- Mandibular Prominence → Lower lip and jaw
- Lining epithelium of nose and respiratory tract is Pseudostratified ciliated Columnar epithelium
- Outer Vestibule lined by Str. Squamous keratinized epithelium

Bones & Cartilages	<ul style="list-style-type: none"> • The nasal bone is a small, flat bone of the skull. It makes up the facial skeleton (viscerocranium) along with the zygomatic bone, maxillae, palatine bones, lacrimal bones, inferior nasal conchae, vomer and mandible. • The nasal bone is located medial to the frontal processes of the maxillae. • The external nose is comprised of both bony and cartilaginous components. The bony part shapes the nose root, formed by the nasal, maxillae and frontal bones. • The cartilaginous part is located inferiorly and is comprised of several alar, two lateral, and one septal cartilage: • Bones support the nasal cavity in front and cartilages support it at the back • Nasal cartilage is Hyaline type • Alar cartilages; major alar cartilage forms the apex of the nose; minor alar cartilages support the ala nasi • Lateral processes of the septal cartilage form dorsum of nose Septal cartilage; bounds the nares medially • The philtrum is formed where the nasomedial (or medial nasal process) and maxillary processes Meet during embryonic development (colloquially known as Hulse lines). When these processes Fail to fuse fully in humans, a cleft lip (sometimes called a “hare lip”) can result. A flattened or Smooth philtrum can be a symptom of Fetal alcohol syndrome or Prader-Willi syndrome. • Most fractured facial bone is nasal Bone
Boundaries of nasal cavity	<ul style="list-style-type: none"> • Nasal cavity extends from nares to choanae (posterior septum) • Floor: Hard palate , Roof: Sphenoid and ethmoid • Medial wall: Septum of nose • Lateral wall: medial orbit, ethmoidal air cells, maxillary sinus
Nerve supply	<ul style="list-style-type: none"> • Lateral & medial posterior superior nasal cavity - from Nasopalatine, maxillary nerve and pterygopalatine ganglion • Anterior ethmoidal from nasociliary nerve • Lateral posterior inferior nasal cavity: from greater palatine nerve • Anterior superior alveolar, from infra-orbital nerve
External nose	<ul style="list-style-type: none"> • External nose is cartilage and fibro fatty tissue • Functions : Breathing +warming + moisturizing air , Filtering air + Smell • Stops during swallowing • Conchae & sinuses increase the Surface area, epithelium is Vascular has cilia and secretes Mucus • Nerve supply: • External nasal (terminal anterior ethmoidal) • Supratrochlear, Infratrochlear, Infra-orbital nerve • Blood supply: • Dorsal nasal artery (ophthalmic) • External nasal (anterior ethmoidal) and Facial (lateral nasal & septal branches)
Lateral wall of nose	<ul style="list-style-type: none"> • Respiratory epithelium – Pseudostratified ciliated Columnar with mucous cells and very vascular

	<ul style="list-style-type: none"> Olfactory epithelium – ciliated nerve cells, Yellowish, on roof & septum, under superior Concha & in sphenothmoidal recess <p style="text-align: center;"><u>Features – Conchae & Meatuses</u></p> <ul style="list-style-type: none"> The lateral wall has three projections called the superior, middle and inferior conchae. The space Below each conchae is called a meatus Sphenothmoidal Recess is small area above superior conchae and it receives the opening of Sphenoidal air sinus Superior meatus: it lies below the superior conchae. It receives the opening of the Posterior ethmoidal sinuses. Optic nerve is related to posterior ethmoidal sinus Middle meatus : it lies below middle conchae and most complex and by far the most Important Bulla ethmoidalis is a smooth rounded mass formed by the middle ethmoidal sinuses. Hiatus semilunaris is curved opening lies below and in front of the bulla and leads Forward into the infundibulum . It is bounded below by the uncinat process of the ethmoid. Maxillary air sinus opens into the hiatus semilunaris below the bulla ethmoidalis. Anterior ethmoidal sinus opens into the hiatus semilunaris in front of the bulla Ethmoidalis. Middle ethmoidal sinus opens on the bulla ethmoidalis. Frontal sinus; opens into the upper part of the hiatus semilunaris Inferior meatus receives the nasal opening of the Nasolacrimal duct which is partially covered by A mucosal fold (valve of Haser or plica lacrimalis).Nasolacrimal duct is derived from endoderm . Woodruff's plexus is a vascular network located on the posterior lateral wall of the inferior meatus of the nasal cavity and it is generally considered to be responsible for posterior epistaxis. Posterior ethmoidal artery most commonly involved <p><u>Blood Supply of Lateral Wall</u> : By branches of both ICA + ECA.</p> <ul style="list-style-type: none"> Inter Carotid Branches supplying Lateral wall are Anterior & Posterior ethmoidal – branches of Ophthalmic artery (branch of ICA) External Carotid Branches supplying lateral wall : Posterior lateral nasal branches from Sphenopalatine artery Greater palatine artery from Maxillary artery Nasal branch of anterior superior dental from Infraorbital artery Branches of facial artery to nasal vestibule Venous Drainage is by Facial Vein and tributaries Lymphatic Drainage Anteriorly to Submandibular L.Ns and posteriorly to Retropharyngeal nodes.
Nasal septum OR Medial wall of nose	<ul style="list-style-type: none"> Medial wall of nose divides the nasal cavity into Right & Left halves. Fleshy external end of the nasal septum is called the columella - made up of cartilage and soft tissue The nasal septum contains bone and hyaline cartilage. It is normally about 2 mm thick. The nasal septum is composed of four structures: Maxillary bone (the crest), Perpendicular plate of ethmoid bone, Septal nasal cartilage, Vomer bone The lowest part of the septum is a narrow strip of bone that projects from the maxilla and the palatine bones and is the length of the septum. This strip of bone is called the maxillary crest; it articulates in front with the septal nasal cartilage, and at the back with the vomer. Blood Supply is shared with lateral wall : from Ethmoidal , facial , Greater palatine arteries Lymph drainage is same as of Lateral wall or nasal cavity <p><u>Clinical Significance</u></p> <p style="text-align: center;"><u>DNS (DEVIATED NASAL SEPTUM) :</u></p> <p>Can be of C / S shaped , Spur type , Anterior deviation or thickening of Septum type. The nasal septum can depart from the centre line of the nose in a condition that is known as a deviated septum caused by trauma. However, it is normal to have a slight deviation to one side. generally stays in the midline until about the age of seven, at which point it will frequently deviate to the right.</p> <p>An operation to straighten the nasal septum is known as a septoplasty.</p>

	<p>A perforated nasal septum can be caused by an ulcer, trauma due to an inserted object, long-term exposure to welding fumes, or cocaine use.</p> <p>There is a procedure that can be of help to those suffering from the perforated septum.</p> <p>A silicone button can be inserted in the hole to close the open sore.</p> <p>The nasal septum can be affected by both benign tumors such as fibromas, and haemangiomas and malignant tumors such as squamous cell carcinoma.</p> <p>Septoplasty is the treatment of Choice till 17 yrs. of age. Submucosal resection / SMR : in adults</p>
Paranasal sinuses	<ul style="list-style-type: none"> • They Lighten skull , warm & moisturize the air. Give resonance to voice • There are 4 pairs , Maxillary and ethmoidal are present at birth. • Frontol is totally absent and develops at 02 yrs. of age. • Maxillary sinus is largest- pyramidal shaped and open into Posterior Hiatus semilunaris in middle meatus. • Infra orbital nerve may be damaged in relation to Maxillary sinus procedures. • Chronic rhinitis is the common cause of Sinusitis • Frontal sinusitis: morning headaches / office headache , fever ,nasal obstruction • Maxillary Sinusitis : Cheek pain , Nasal blockade , fever , history of flu / URTI.
Key facts	<p><u>Cleft lip:</u></p> <ul style="list-style-type: none"> • multifactorial genetic disorder that involve neural crest cell • The most common congenital anomaly of head is cleft lip > cleft palate • Cleft lip result when the maxillary prominence fail to fuse with Medial nasal prominence • The underlying mesoderm and neural crest fail to expand, resulting in persistent labial Groove • If the medial part of upper lip incompletely formed (median cleft) than orbicularis oris Muscle will insert on ala of the nose <p><u>Cleft palate:</u></p> <ul style="list-style-type: none"> • multifactorial genetic disorder that involve neural crest cell • Cleft palate is classified into anterior and posterior type on the basis of incisive foramen • Anterior cleft palate occurs when palatine shelves fail to fuse with primary palate • Posterior cleft palate occurs when palatine shelves fail to fuse with each other and with nasal septum • The infant may be unable to Suck properly. Feeding difficulty occur more <ul style="list-style-type: none"> • Posterior choanae is the narrowest part of Nasal cavity. • Tip of nose is supported by Columella and supplied by Ophthalmic division of CNV. • Person develops severe temporal headache. there are vesicles on medial side of eye ala of nose in ophthalmic nerve involvement • Nasal cilia beat at 10-HZ frequency • Sesamoid Cartilage is present in : Ala of nose > Trachea • Ectopic sebaceous glands seen in Palate • Sphenopalatine artery is called the artery of Epistaxis –(nosebleed) • Little's Area contains Plexus which bleeds most commonly (involved in anterior epistaxis) • For Posterior Epistaxis : Woodruff's plexus (posterior ethmoidal artery bleeds commonly) • Management of epistaxis : Pinch the nose with thumb and index finger while sitting on stool , anterior & posterior nasal packaging (Foley's catheter may be used in posterior packing) . Ligation of Ascending pharyngeal artery and Maxillary artery • Juvenile angiofibroma presents with profuse epistaxis in teenagers (14 , 16 yrs. of age) • Rhinopyoma (potato tumor) - tumor of sebaceous glands of nose. managed by medial maxillectomy. • When furuncle or boil over the nose is squeezed or permanently incised, infection can spread to cavernous sinus leading to Thrombosis. • Ethmoid is the key area in the disease causation and act as a reservoir of infection • Histologically Ethmoidal polyps are of two types' i-e neutrophil type and eosinophils type. • CSF rhinorrhoea: Leakage of CSF into the nose. The most common site of leak is cribriform plate • Beta-2 transferrin: protein seen in CSF and not in nasal discharge, indicator of CSF leak • Child with blood-stained discharge from nose & Nasal obstruction → foreign body Nose

ARTERIAL SYSTEM OF HEAD & NECK

Aortic arch	<ul style="list-style-type: none"> It gives: <ul style="list-style-type: none"> ✓ Brachiocephalic trunk (1st branch), left Common Carotid (2nd), and Left Subclavian artery (3rd branch) Right side: Brachiocephalic artery (or brachiocephalic trunk or innominate artery): Aortic arch at the level of brachiocephalic artery arises at second right costal cartilage. Then it runs upwards to the right and at the border of the right sternoclavicular joint divides into Right Subclavian artery & Right CCA. Left sided CCA arises directly from arch of aorta, just a little away from midline. Common variation in the arteries arising from arch of the aorta is that left CCA arising from brachiocephalic trunk 		
Internal carotid artery	<ul style="list-style-type: none"> At its origin ICA is lateral to external carotid artery then goes posteriorly to become medial in the rest of the course. Lateral to optic Chiasma terminates into anterior and middle cerebral artery. 		
External carotid artery	<ul style="list-style-type: none"> Begins at the level of upper border of thyroid cartilage Terminate in the substance of parotid gland into superficial temporal artery and maxillary artery Behind the neck of mandible. ECA gives all branches in neck External carotid artery branches: <ol style="list-style-type: none"> Superior thyroid artery (Anterior) Medial branch: Ascending Pharyngeal artery Lingual artery : Anteriorly it runs obliquely deep to posterior digastric near palatoglossus muscle Facial artery- Anterior Occipital artery-Posterior Posterior auricular artery-Posterior Terminal branches : Maxillary artery + Superficial Temporal artery accompanied by Auriculotemporal 		
Branches of Maxillary artery	1st part (5 branches) <ol style="list-style-type: none"> Middle meningeal artery, Accessory meningeal Anterior tympanic branch Deep auricular branch inferior alveolar artery 	2nd part (4 branches) <ul style="list-style-type: none"> Masseteric Deep temporal Buccal Pterygoid branches 	3rd part (6 branches) <ul style="list-style-type: none"> Posterior superior alveolar Infra orbital Greater palatine Pharyngeal Artery to pterygoid canal Sphenopalatine (terminal branch)

Carotid Endarterectomy:

- Loss of cervical nerve sensation is always present after carotid Endarterectomy but tends to improve with time. When disregarding the frequently injured Cutaneous cervical Nerve, the nerves at potential risk include facial, Glossopharyngeal, vagus, accessory, and Hypoglossal nerve. The hypoglossal nerve appears to be the most susceptible to injury because of its proximity to carotid bifurcation followed by vagal nerve injury
- Compression of the facial artery on one side doesn't stop bleeding from a lacerated facial Artery of one of its branches that's why in laceration of lip.
- Pressure must be Applied on both Sides of the cut to stop bleeding from facial artery bilaterally.

VERTEBRAL ARTERY	<ul style="list-style-type: none"> The vertebral arteries arise from the subclavian arteries, one on each side of the body It enters deep to the transverse process at the level of the 6th cervical vertebrae <p>Branches:</p> <ol style="list-style-type: none"> Anterior spinal artery: (ASA) arises from branches of the vertebral arteries and courses along the anterior aspect of spinal cord. Occlusion of ASA leads to Medial Medullary syndrome Medial Medullary syndrome presents with a lesion of the hypoglossal nerve (deviation of Tongue on protrusion toward the side of lesion) and lesions to the medial lemniscus and the corticospinal tract
-------------------------	---

	<p>2. PICA</p> <p>The posterior inferior cerebellar artery (PICA), the largest branch of the vertebral artery. It supplies dorsolateral surface of medulla.</p> <p>PICA gives posterior spinal artery (PSA). Occlusion of PICA leads to lateral Medullary syndrome.</p> <p>Lateral Medullary (Wallenberg) syndrome: The cranial nerve nuclei involved in this lesion are the vestibular or cochlear part of CN 8 (May produce nystagmus, vertigo, Nausea, and vomiting), Glossopharyngeal nerve (result in diminished or absent gag reflex) and the vagus nerve (may produce dysphagia, or hoarseness), and the spinal nucleus tract of CN 5.</p> <p>The long tracts involved are the Spinothalamic tract and the descending Hypothalamic fibres.</p>
BASILAR ARTERY	<p>The two vertebral arteries join to form the basilar artery. Occlusion leads to Medial Pontine syndrome. Locked-in Syndrome, Quadriplegia & Coma may occur in Basilar artery thrombosis.</p> <p>Medial pontine syndrome: lesion affects the exiting fibres of the Abducent nerve (result in Diplopia on attempted lateral gaze to the affected side) and the Corticospinal tract.</p> <p>Anterior inferior cerebellar artery (AICA) is a branch of basilar artery.</p> <p>Labyrinthine artery: The labyrinthine artery is a long slender branch of the AICA (85 %) or basilar artery. Occlusion leads to lateral pontine syndrome.</p> <p>Lateral pontine syndrome: The cranial nerve involved will be the facial (produces ipsilateral facial paralysis, loss of taste from anterior 2/3 of the tongue, loss of lacrimation and salivation and loss of corneal reflex) and vestibulo-cochlear in the Caudal pons, the trigeminal nerve in the rostral pons and the spinal nucleus and Tract of CN V in both lesions.</p> <p>AICA Poop Face: Face involvement is seen in AICA syndrome. No facial involvement in PICA occlusion.</p> <p>Posterior cerebral arteries</p> <p>The basilar artery terminates by splitting into the left and right posterior Cerebral arteries.</p> <p>The posterior cerebral artery supplies the occipital lobe (visual area), the inferior part of the temporal lobe, and various deep structures including the thalamus, Epithalamus, mid brain and nearby areas.</p>

INTERNAL CAROTID ARTERY

- Contributes 80% blood supply to head and neck. Entering the cranial cavity, each internal carotid artery gives off the:
- Ophthalmic artery and Posterior communicating artery:
- Basilar artery and ICA communicate with each other by posterior communicating artery
- The posterior communicating artery runs back from the internal carotid artery above the Oculomotor nerve and anastomoses with posterior cerebral artery (a terminal branch of the basilar artery)

1. Middle cerebral artery:

- The middle cerebral artery is the largest branch of the internal carotid
- It supplies **bulk of the lateral surface of the hemisphere**; except for the superior inch of the frontal and parietal lobe (anterior cerebral artery), and the inferior part of the temporal lobe.
- Also supplies the Anterior temporal lobes and the insular cortices, primary motor and sensory areas of the Face, throat, hand, and arm, and in the dominant hemisphere, the areas for speech.
- Broca's area + Wernicke's area (Superior temporal gyrus)
- Deep branches supply the basal ganglia as well as the internal capsule
- Arterial supply of motor area of cerebral cortex is by both anterior and middle Cerebral artery

MCA occlusion site and resulting Aphasia

- ✓ Global aphasia -trunk of MCA involved
- ✓ Broca's aphasia -anterior branch of MCA involved
- ✓ Wernicke's aphasia – posterior branch of MCA involved.

2. Anterior cerebral artery:

- ACA along with the middle cerebral artery forms at the Termination of the internal carotid artery.
- Supplying the ventral half of the anterior limb of the internal capsule supplying the pre-frontal area.
- This is the area of mentality and inhibition of Primitive reflexes.

- Supplies the motor and sensory areas of the Lower limb, and the paracentral Lobule (cortical bladder centre), corpus callosum + Cingulate gyrus

3. Anterior choroidal artery:

- The most distal branch of the ICA, originates just after the origin of the posterior communicating artery, and courses Posterolaterally to supply Anterior medial temporal lobe, optic tract, Geniculate body, medial globus Pallidus, medial third of the cerebral peduncle, portions of the ventral and pulvinar Thalamus and the posterior limb of the internal capsule

KEY FACTS

- Superior + Lateral surface of Cerebral Hemispheres (Frontal , Parietal lobes) → MCA
- Medial & inferior surface of Hemispheres (temporal , parietal) → ACA
- Posterior part of Hemi- sphere + Occipital area , mid brain , thalamus → PCA
- Basal Ganglia + Inter capsule : by both MCA + ACA > MCA > ACA
- Insular cortex , Taste + Speech areas , Somatosensory area : MCA
- Secondary somaesthetic area : ACA
- Leg Area : ACA. ; Rest all of the Body except Leg area : MCA
- MC site of hypertensive haemorrhage : Putamen nucleus → lenticulo striatal arteries involved
- Major artery entering and supplying brain : ICA
- Circle of Willis is formed by 2 Vertebral + 2 ICA, while Circle of Willis connects Basilar artery & ICAs**

VENOUS SYSTEM

Internal jugular vein (IJV)	<ul style="list-style-type: none"> it starts as continuation of the sigmoid venous sinus and leave the skull through jugular Foramen. The internal jugular vein is the biggest vein of the neck. The right internal jugular Vein is generally bigger compared to the left it is closely related with deep cervical lymph nodes during whole course it runs from ear lobules to Sternoclavicular joint Unites with subclavian vein behind the middle of clavicle and form the brachiocephalic vein IJV after leaving Jugular foramen has immediate relation with ICA whereas inside Jugular foramen related to CN XI <p>Tributaries:</p> <ul style="list-style-type: none"> Inferior Petrosal vein, Pharyngeal, Lingual , Middle thyroid , Superior thyroid vein, Facial vein
External jugular Vein (EJV)	<ul style="list-style-type: none"> Begins on the surface of Sternocleidomastoid behind angle of jaw, in the substance of parotid Formed by union of posterior auricular vein and posterior division of Retromandibular vein After its formation, it runs downwards over the sternocleidomastoid, and reaches the Posterior border of the muscle about an inch above the clavicle. There, it pierces the deep fascia, and descends close to SCM to End in the subclavian vein behind the middle clavicle. It has valves <p><u>Tributaries: PAST</u></p> <ol style="list-style-type: none"> Posterior external jugular vein Anterior jugular vein—terminal tributary of EJV, which join subclavian vein Suprascapular vein Transverse cervical vein
Subclavian vein	<ul style="list-style-type: none"> It is the continuation of Axillary vein at the outer border of the first rib It joins the internal jugular vein to form brachiocephalic vein and receives the EJV It often receives the thoracic duct on the left side and the right lymphatic duct on Right side
Retromandibular vein	<ul style="list-style-type: none"> Formed from union of maxillary vein and superficial temporal vein. Retromandibular vein divides into anterior and posterior division Posterior division joins posterior auricular vein and form EJV which drain into subclavian vein. Anterior division joins facial vein and drain into IJV.

	<ul style="list-style-type: none"> o Facial vein forms at medial angle of eye from union of supraorbital and supratrochlear veins
Key Facts	<ul style="list-style-type: none"> o Infection from middle ear may spread to IJV o Surgical removal of deep cervical node can puncture IJV o For Central venous line or catheter most often use Right IJV o The RJV is preferred over the left-sided internal jugular vein (LIJV) because cannulation of o The LJV is more difficult and associated with a higher complication rate o Compression of both jugular vein cause intracranial pressure to raise, and, then falls o Infection to cavernous sinuses spreads via Superior Ophthalmic Vein > inf Ophthalmic vein

CRANIAL NERVES

(CN 2, 3, 5, 7, 10 are imp for exams)

- Total CN = 12 , may be pure sensory , Pure Motor or mixed nerve
- 1.Olfactory nerve. 2. Optic nerve (SSA)
- Origin from mid brain- : CN- Three (Oculomotor) from front and 4th CN from back/posterior of brainstem
- Only nerve to arise from Posterior surface of Brain stem is trochlear nerve or 4th CN
- Origin from Pons : CN 5 , 6 , 7 , 8
- CN5 = Trigeminal Nerve , CN6= Abducent, CN7= Facial, CN8= Vestibulocochlear Nerve
- Origin from medulla oblongata- : CN 9,10,11,12
- CN 9 = Glossopharyngeal , CN10= VAGUS , CN11= Accessory Cranial , CN12= Hypoglossal nerve
- Sensory Cranial Nerves : CN 1,2,8 or Cranial nerve which contain only afferent (Sensory) fibres : CN 1,2,8
- Motor Cranial Nerves : CN 3,4,6, 11,12.
- Cranial nerve which contain only efferent (motor) fibres : 3, 4,6, 11, 12
- Mixed Sensory (Efferent) & Motor (afferent) CN-5, 7,9, 10 → mixed
- Only two nerves decussate : CN 2 & CN 4
- CN 6,8,12 lie in floor of 4th ventricle (6th CN is in midline and centre of body)
- Parasympathetic cranial nerve CN 3,7,9,10
- Smallest CN with Longest Intra-Cranial Course and Emerging from Dorsal Aspect of Brainstem : Trochlear
- Trigeminal : Largest Cranial Nerve and Thickest Cranial Nerve
- Cranial Nerve with Direct Projection to Cerebral Cortex---Olfactory
- Cranial Nerve with Longest Intra-Osseous Course : Facial
- Cranial Nerve affected in Pyogenic Meningitis is CN 8
- Cranial Nerve affected in Tuberculous Meningitis : CN 3
- CN 3 also affected mostly in DM and can affect posterior communicating artery
- Cranial Nerve affected in Multiple Sclerosis : Optic Nerve.
- Cranial nerve affected in Sarcoidosis : CN 7 , also in Bell's palsy
- **Solitary Nuclei** is a series of purely sensory nuclei that receives the axon of all general and special visceral afferent fibres carried into the CN 7 , 9 , 10
- **Nucleus Ambiguus** is a group of large motor neurons, situated deep in the Medullary reticular formation. Axon arising from cells in this nucleus course in the cranial nerves 9+ 10
In CN X these fibres supply muscle of the soft palate, larynx. Pharynx and upper Esophagus.

Olfactory nerve (CN I)	<ul style="list-style-type: none"> • Passes through Perforations in cribriform plate of ethmoid bone • Neurons are Bipolar type and sense of smell by passes the thalamus • Only neuron that can regenerate and replaced by stem cell • These are unmyelinated C-fibres (smallest and slowest) • Mitral cell are present in olfactory bulb • Olfactory epithelium contain Bowman glands. Olfactory epithelium possess non-ciliated epithelium which act as receptor for odour. Sharp order have the quality of water and lipid solubility • Odorant molecule binds to receptor, activation of G protein → opening of Na/Ca channels → depolar. • Olfactory area location -- anterior perforating substance
-------------------------------	--

	<ul style="list-style-type: none">Primary Olfactory cortex is in posterior inferior temporal gyrus, Uncus (AKA pyriform bulb)															
CN II, III, IV, VI	<ul style="list-style-type: none">They have been Explained earlier in this section (see EYE)															
Trigeminal nerve (CN V)	<p>Trigeminal nuclei = 4</p> <ul style="list-style-type: none">Motor nucleus in Pons medial to main sensory nucleus - supplies mastication musclesMain sensory nucleus in Pons , lateral to the motor nucleus it receives tactile and pressure sensation from the face, scalp, oral + nasal cavity and duraSpinal trigeminal nucleus: It is the caudal continuation of the main sensory nucleusMesencephalic nucleus: in the point of entry of the 5th nerve and extend into midbrain It receive proprioceptive input from joints, muscle of mastication, Extraocular muscles, Teeth and the Periodontium Some of these fibres synapse monosynaptically motor neurons, forming the sensory Limb of the jaw jerk reflex. Lesion of Mesencephalic nucleus will result in diminished jaw jerk reflex <p>Trigeminal Nerve Divisions = 3 main (Ophthalmic , Maxillary & Mandibular nerve)</p>															
Ophthalmic nerve (CN V1)	<p>It supplies the skin of the forehead, the upper eyelid, conjunctiva Side of the nose including tip. Following branches of the nerve pass to the skin</p> <ul style="list-style-type: none">Lacrimal nerve supplies the skin and conjunctiva of the lateral part of the upper eyelidExternal nasal nerve : It supplies skin of the tip of noseFrontal nerve: it gives supraorbital and supratrochlear nerves supraorbital nerve supplies the skin and conjunctiva on the central part of the upper eyelid; it also supplies the skin of the forehead and the Mucous Membrane of the frontal air sinus The supratrochlear nerve supplies skin and conjunctiva on the medial part of the upper Eyelid and the skin over the lower part of the forehead, close to the median planeNasociliary nerve arises from the ophthalmic division of the trigeminal nerveBranches of Nasociliary nerve : communicating branch to the ciliary ganglion is a sensory nerve , long ciliary nerves ,Posterior ethmoidal nerve , Infratrochlear nerve and Anterior ethmoidal nerve															
Maxillary nerve (CN V2)	<ul style="list-style-type: none">Pain between eyes, lips and auricular area is carried by maxillary nervesupplies the skin on the posterior part of the side of the nose, the lower Eyelid, the cheek, the upper lip and lateral side of the orbital opening. Branches are as follows; <table><tr><td>In Cranium</td><td><ul style="list-style-type: none">Middle meningeal nerve from the pterygopalatine fossa:Zygomaticofacial nerve: supplies skin over the prominence of cheekZygomaticotemporal nerveNasopalatine nerve--through the Sphenopalatine nerveGreater and lesser PalatinePosterior superior alveolar nerve and Pharyngeal nerve</td></tr><tr><td>In infraorbital foramen</td><td><ul style="list-style-type: none">Anterior superior alveolar nerve, Middle superior alveolar nerveInfraorbital nerve is a direct continuation of the maxillary nerve. It immediately divides into numerous small branches, which radiate out from the foramen and supply the skin of lower eyelid and cheek side of the nose and the upper lip.Maxillary sinus is supplied by superior alveolar nerve and the infraorbital nerve</td></tr><tr><td>In the Face</td><td><ul style="list-style-type: none">Inferior Palpebral nerve, Superior labial nerve and Lateral nasal nerve</td></tr></table>	In Cranium	<ul style="list-style-type: none">Middle meningeal nerve from the pterygopalatine fossa:Zygomaticofacial nerve: supplies skin over the prominence of cheekZygomaticotemporal nerveNasopalatine nerve--through the Sphenopalatine nerveGreater and lesser PalatinePosterior superior alveolar nerve and Pharyngeal nerve	In infraorbital foramen	<ul style="list-style-type: none">Anterior superior alveolar nerve, Middle superior alveolar nerveInfraorbital nerve is a direct continuation of the maxillary nerve. It immediately divides into numerous small branches, which radiate out from the foramen and supply the skin of lower eyelid and cheek side of the nose and the upper lip.Maxillary sinus is supplied by superior alveolar nerve and the infraorbital nerve	In the Face	<ul style="list-style-type: none">Inferior Palpebral nerve, Superior labial nerve and Lateral nasal nerve									
In Cranium	<ul style="list-style-type: none">Middle meningeal nerve from the pterygopalatine fossa:Zygomaticofacial nerve: supplies skin over the prominence of cheekZygomaticotemporal nerveNasopalatine nerve--through the Sphenopalatine nerveGreater and lesser PalatinePosterior superior alveolar nerve and Pharyngeal nerve															
In infraorbital foramen	<ul style="list-style-type: none">Anterior superior alveolar nerve, Middle superior alveolar nerveInfraorbital nerve is a direct continuation of the maxillary nerve. It immediately divides into numerous small branches, which radiate out from the foramen and supply the skin of lower eyelid and cheek side of the nose and the upper lip.Maxillary sinus is supplied by superior alveolar nerve and the infraorbital nerve															
In the Face	<ul style="list-style-type: none">Inferior Palpebral nerve, Superior labial nerve and Lateral nasal nerve															
Mandibular nerve (CN V3)	<p>It is a mixed Nerve and the largest of three divisions of the trigeminal nerve. All branches of the mandibular nerve originate in the infratemporal fossa</p> <p>Branches</p> <table><tr><th>From Main trunk</th><th>From Anterior division</th><th>From Posterior division</th></tr><tr><td>✓ Meningeal branch</td><td>✓ Masseter</td><td>✓ Auriculotemporal nerve</td></tr><tr><td>✓ Nerve to medial pterygoid</td><td>✓ Deep temporal</td><td>✓ Lingual nerve</td></tr><tr><td></td><td>✓ Nerve to lateral pterygoid</td><td>✓ inferior alveolar and mylohyoid nerve</td></tr><tr><td></td><td>✓ Buccal nerve</td><td></td></tr></table>	From Main trunk	From Anterior division	From Posterior division	✓ Meningeal branch	✓ Masseter	✓ Auriculotemporal nerve	✓ Nerve to medial pterygoid	✓ Deep temporal	✓ Lingual nerve		✓ Nerve to lateral pterygoid	✓ inferior alveolar and mylohyoid nerve		✓ Buccal nerve	
From Main trunk	From Anterior division	From Posterior division														
✓ Meningeal branch	✓ Masseter	✓ Auriculotemporal nerve														
✓ Nerve to medial pterygoid	✓ Deep temporal	✓ Lingual nerve														
	✓ Nerve to lateral pterygoid	✓ inferior alveolar and mylohyoid nerve														
	✓ Buccal nerve															

	<ul style="list-style-type: none"> • Lingual Nerve originates in the infratemporal fossa and passes anteriorly into the floor of the oral cavity by passing through the gap between the Mylohyoid, superior constrictor & Middle constrictor muscles. • As it travels through the gap, it passes Inferior to attachment of superior constrictor to the mandible and continues the medial surface of the mandible adjacent to the last molar tooth deep to gingiva. • Here, it can be palpated against the bone by Placing a finger into the oral cavity. It is Joined by Chorda tympani and supplies anterior 2/3rd of tongue. It Also gives pre-ganglionic secretomotor fibres to submandibular gland • Inferior alveolar nerve lies in mandibular canal • Mylohyoid nerve: branch of inferior alveolar that supplies Anterior belly of digastric muscle
--	--

VAGUS NERVE

- It is the longest cranial nerve having Longest Extra-Cranial Course.
- Pass posteriorly within carotid sheath between IJV and ICA
- Bilateral cutting of vagus nerve cause death
- The vagus nerve provide 75% of all parasympathetic outflow
- 80% of the vagus nerve fibre deliver information from enteric nervous system.
- Vagus nerve and thoracic sympathetic nerve end in transverse two third and lateral one-third Junctions.
- It lies Posterior to the root of both lungs
- Dorsal nucleus of vagus is the major parasympathetic nucleus lies lateral to rhomboid fossa or Sulcus limitans i.e it lies in the upper medulla anterior to the floor of 4th ventricle
- If the Vagus nerve is cut proximally, the stimulation of central part will cause apnea

FACIAL NERVE

Arises from lateral pons, begins in internal auditory canal to terminate at stylomastoid foramen. It is a mixed nerve.

Branches	Intracranial or in facial canal (CNG)	<ul style="list-style-type: none"> • Chorda tympani: it exits the skull and enters infratemporal Fossa through medial end of the petrotympanic fissure. • Nerve to stapedius • Greater Petrosal nerve • Lesion to facial nerve in facial canal will cause facial deviation along with loss of Sensation from anterior 2/3 of tongue. • Facial canal is the longest bony canal of any nerve
	At stylomastoid foramen	Extracranial branches are: <ul style="list-style-type: none"> • Posterior auricular muscle – 1st extracranial branch of the facial nerve • Nerve to Posterior belly of digastric muscle • Nerve to Stylohyoid muscle
	In the Face	Five terminal branches. <ul style="list-style-type: none"> • Temporal, Zygomatic, buccal, marginal mandibular and cervical branch Zygomatic branch supplies orbicularis oculi (medial Palpebral ligament attach to it) Cervical branch supplies platysma (subcutaneous muscle)
Clinical anatomy	<ul style="list-style-type: none"> • Internal auditory meatus has Facial nerve and vestibulo-cochlear nerve • Facial nerve enter temporal lobe through this internal auditory meatus • The facial nerve forms internal genu • Ramsay Hunt syndrome (herpes zoster oticus) occurs when a shingles outbreak affects the Facial nerve near one of your ears • Chorda tympani is the branch of facial nerve carrying taste sensations from ant 2/3rd tongue – SVA fibres • Tympanic nerve arises from Glossopharyngeal nerve • Lower one third of pons contains facial nucleus 	

FACIAL NERVE PARALYSIS

- Most commonly effect the muscle of fascial expression, lacrimation (dry eye), corneal Reflex (can't blink), taste of anterior 2/3rd of tongue and sound damping (Hyperacusis)
- Common cause of unilateral congenital facial palsy is birth trauma related to a difficult delivery.
- Risk factors includes forceps delivery, birth weight of more than 3500 gm and primiparity
- Forehead involvement should be assessed by asking the patient to raise the eyebrows

Causes of fascial nerve paralysis:

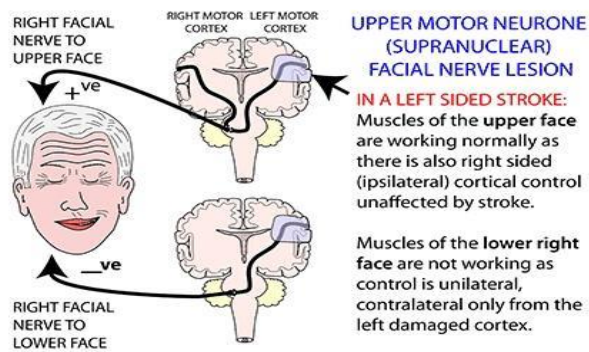
Supranuclear lesion (UMNL)	<ul style="list-style-type: none"> • Forehead is normal i.e., can wrinkle • Infarct to face area of motor cortex homunculus (MCA) • Infarct to internal capsule (lacunar stroke) • Infarct to pons (CN VII nucleus)
Infranuclear lesion (LMNL)	<ul style="list-style-type: none"> • forehead is paralyzed = No wrinkle • Bell-palsy (linked to HSV so treated with steroids and acyclovir) • Lyme disease and Gullian Barr syndrome both has bilateral facial palsy • Herpes zoster oticus (Ramsay-Hunt syndrome) – unilateral facial palsy External auditory canal defect and ear pain • Sarcoidosis, tumor (acoustic neuroma) and DM

KEY CONCEPT

Grab this concept to avoid confusion.

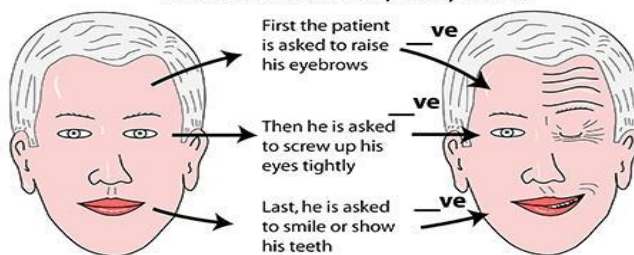
- ✓ **Facial muscle Paralysis** : The facial muscles are innervated by facial nerve
Causes: Damage to facial N. (by a tumor in internal acoustic meatus or parotid gland) /or Operation or infection in middle ear / or Perineuritis, Bell's palsy in facial nerve canal.
- ✓ **Results : Lower motor neuron lesion which Involves distortion of face + drooping of lower** Eyelid + angle of mouth will sag on the Affected side. /
- ✓ **But Upper motor neuron lesion is due to lesion of pyramidal tract and here the upper face is normal** because the neurons Supplying this part receive corticobulbar Fibres from both cerebral cortices.
- ✓ **Pt Can Wrinkle in UMNL/Supranuclear Lesion (or palsy)**
- Transverse Fracture of Petrous temporal bone causes facial palsy in 50 % cases.
- But Longitudinal fractures are more common, and they carry 10 to 15 % chance of facial palsy
- **Bell's Palsy** is the Idiopathic Ipsilateral facial muscle paralysis.
- Not every facial paralysis is Bell's palsy.
- Remember the Facial Expressions**
- Surprise : Frontalis muscle, while for Doubt : Mentalis
- **Horror, terror, and fight : Platysma**
- Smiling and laughing: Zygomatic major, while, for contempt: Zygomatic minor
- Grief : Depressor anguli oris, but, for Anger : Dilator naris and depressor septi

FACIAL NERVE LESIONS



ALL MOVEMENTS ARE MISSING IN THE RIGHT SIDE OF THE FACE INDICATING A "LOWER MOTOR LESION"

3 functions are tested separately in turn:



Causes of lower motor neurone lesions include Bell's palsy, middle ear infections, multiple sclerosis, acoustic neuroma, herpes zoster, diabetes, sarcoid, temporal bone fractures

Lesion Site	Effects
at or above stylomastoid foramen	all facial muscle paralysis or bell's palsy
in facial/middle ear canal above origin of chorda tympani	facial muscle paralysis + loss of taste sensation
above the origin of nerve to stapedius	above symptoms + hyperacusis
at geniculate ganglion	all above symptoms + loss of lacrimation

SYMPATHETIC GANGLIA OF HEAD & NECK

Superior Cervical Ganglion	Middle Cervical Ganglion	Inferior Cervical Ganglion
<ul style="list-style-type: none"> Anterior to lateral Mass of C1 & C2 3cm long somatic branches -- (C1-4) Branches to internal & external carotid arteries 	<ul style="list-style-type: none"> At C6, medial to carotid tubercle Anterior to vertebral artery 2 somatic branches -- (C5,6) Branches to inferior thyroid and subclavian arteries 	<ul style="list-style-type: none"> At C7, behind vertebral artery 1cm x 0.5cm on neck of 1st rib 2 somatic branches -- (C7,8) Branches to vertebral artery

CERVICAL PLEXUS

- Formed by the anterior rami of cervical nerves C2 to C4, and possibly a Contribution from the anterior ramus of C1
- Plexus forms in the substance of the muscles making up the floor of the posterior triangle within the Prevertebral layer of cervical fascia.
- consists of: Muscular (or deep) branches and Cutaneous (or superficial) branches
- **Muscular (or deep) branches** supply prevertebral and lateral vertebral Muscles, including the rectus capitis anterior, rectus capitis lateralis, longus coli, and Longus capitis
- **Cutaneous (superficial) branches** of the cervical plexus are visible in the posterior triangle as they Pass outward from the posterior border of the sternocleidomastoid muscle
 1. The lesser occipital nerve : from Ventral or anterior rami of cervical nerve C2.
 2. The great auricular nerve consists of C2, C3 and supplies angle of mandible
 3. **Transverse cervical nerve** consists of branches from the cervical nerves **C2 and C3**
 4. The supraclavicular nerves are group of cutaneous nerves from C3 and C4 that, after emerging from beneath the posterior border of SCM, descend and supply the skin over the clavicle and shoulder as far inferiorly as rib
- NOTE : **greater auricular nerve & lesser occipital are branches of cervical plexus**
- **Greater occipital nerve** is the branch of the **posterior/dorsal ramus of the C2,C3** nerve. Not A branch of cervical plexus
- **Ansa (Loop) Cervicalis** is a nervous loop situated in front of the carotid sheath.
It formed by Union of two limb
Superior limb: descending from hypoglossal nerve and containing fibres of C1 spinal Nerve
Inferior limb: from C2 and C3

LYMPHATIC DRAINAGE OF HEAD & NECK

Parotid lymph nodes	<ul style="list-style-type: none"> ○ Situated on or within the parotid gland. ○ Receive lymph from scalp above the parotid gland, eyelids, auricle, and external auditory meatus
Submandibular lymph nodes	<ul style="list-style-type: none"> ○ Lies superficial to the submandibular salivary gland just below the body of mandible. ○ Receive lymph from Front of the scalp, nose, cheek, upper and lower teeth (except lower incisor) frontal + maxillary + Ethmoid sinus, Anterior 2/3rd of tongue except tip, floor of mouth, vestibule, and gums.
Submental lymph nodes	<ul style="list-style-type: none"> ○ Lies in submental triangle just below the chin. ○ They receive lymph from the tip of tongue, the floor of anterior part of mouth, central part of lower lip and the skin over the chin
Deep cervical lymph nodes	<ul style="list-style-type: none"> ○ Arranged in a vertical chain along the course of internal jugular vein within the carotid Sheath. ○ Efferent lymph vessels from all the deep cervical lymph nodes join to form the jugular Trunk, which drains into the thoracic duct or right lymphatic duct. ○ Jugulo-digastric nodes lie behind angle of the jaw and drains the tonsil. ○ Jugulo-Omohyoid is mainly associated with lymph drainage of the tongue

HEAD & NECK BCQS – ONE LINERS

1. Midline cleft lip is failure of fusion of two medial nasal processes (not Prominences)
2. Unilateral cleft lip : failure of fusion of median nasal process with maxillary process
3. Cleft palate → failure of fusion of lateral palatine process nasal septum and median palatine process.
4. Most Common congenital anomaly of head and neck is cleft lip and cleft palate both.
5. Superior Thyroid artery arises from: External Carotid Artery
6. Otic ganglion is between mandibular nerve and tensor tympani.
7. Its superior border is formed by: Foramen Ovale.
8. About swallowing wrong is = depression of soft palate
9. Regarding Pterygopalatine Raphe: Buccinator Attaches to it
10. Pretracheal fascia infections spreads to Anterior mediastinum
11. Surgery on Submandibular gland which has more chances of injury to marginal mandibular nerve.
12. Which ligament supports odontoid process of axis on atlas : Transverse ligament
13. Skin over the tip of the nose is supplied by : External nasal branch of V1 > Nasociliary nerve.
14. Ligation of Superior laryngeal artery may damage which nerve : internal laryngeal nerve
15. Which of the following is accompanied with optic nerve in optic canal : Ophthalmic artery
16. Digastric triangle is bounded by both belly of digastric and mandible
17. Posterior tongue is drained by Jugulo-omohyoid → deep cervical lymph nodes
18. Fascia deep to parotid gland forms: Stylomandibular ligament
19. Patient is unable to open his mouth: Medial pterygoid involved
20. Which muscle gets paralyzed/damaged in temporomandibular joint dislocation : Lateral pterygoid
21. Isthmus of thyroid is situated over which tracheal rings : 2,3,4
22. Narrowest point in paediatric airway: Cricoid
23. Pretracheal fascia: Completely encircles thyroid
24. Which gland is not surrounded by deep cervical fascia : Sublingual
25. Internal carotid artery at bifurcation is -- lateral to external carotid artery then turns medially and posteriorly.
26. Retromandibular vein is formed by junction of Maxillary vein and Superficial temporal vein
27. Masseteric fascia derived from Superficial layer of Deep cervical fascia
28. Most common salivary gland tumor is of which salivary gland: Parotid gland
29. Trachea commences at C6.
30. Deep to posterior digastric and near palatoglossus a structure runs obliquely upwards : Lingual artery
31. What is correct about thyroid: Isthmus attached to cricoid
32. Gustatory sweating is caused by: Superficial Parotidectomy
33. Maxillary sinus opens in -- middle meatus.
34. Naso lacrimal duct opens in inferior meatus.
35. About thyrohyoid membrane false is its inferior free margin form vestibular ligament.
36. Abductor of vocal folds is -- posterior cricoarytenoid muscle.
37. About Posterior Triangle of Neck what is true: Contains subclavian artery & three trunks of brachial plexus.
38. Internal carotid bleeding stopped by compressing: C6
39. Only intrinsic laryngeal muscle supplied by external laryngeal nerve. : cricothyroid muscle.
40. Anterior 2/3 of tongue supplied by general sensation by Lingual nerve
41. External jugular vein is formed by the union of posterior division of retromandibular + posterior Auricular vein
42. Thyrocervical trunk is the branch of 1 st part subclavian artery
43. Costocervical trunk is the branch of 2 nd part of subclavian artery
44. Great vein of Galen drained into straight sinus
45. Duct of parotid gland is opposite to upper 2 nd molar tooth
46. Derivative of 2 nd branchial arch : posterior belly of digastric
47. Prevertebral fascia extended up to T4
48. Dangerous area of Scalp : Loose areolar tissue / 4 th layer.
49. Patient has bitemporal hemianopia , lesion is at -- Central or Middle chiasma.
50. Nerve accompany superficial temporal artery is -- Auricular temporal nerve.
51. Ophthalmic artery is a branch of -- internal carotid artery.
52. About nerve supply of larynx: sensory supply above vocal folds by internal laryngeal nerve.
53. sensory supply below vocal cords by -- recurrent laryngeal nerve.

54. All are elevators of larynx, except -- omohyoid muscle
55. Posterior belly of digastric muscle is supplied by facial nerve
56. Sternocleidomastoid muscle is supplied by Spinal accessory nerve
57. Internal jugular vein is direct continuation of -- sigmoid sinus
58. Nerve supply of orbicularis oculi : Zygomatic branch of facial nerve
59. A girl has problem in opening mouth. Which muscle is defected: Lateral pterygoid
60. Lateral to carotid artery: internal Jugular vein
61. Pt had nodule on ant 2/3 of tongue, lymphatic drainage is: Submandibular
62. On autopsy of CRF patient which organ was hypertrophied : Para thyroid glands
63. Intraarticular disc of TMJ involved, Muscle paralyzed is: Lateral pterygoid
64. Hypoglossal nerve injured → Tongue deviated to same side
65. Superior thyroid artery is related to external laryngeal nerve
66. Maxillary nerve leaves the skull through foramen rotundum
67. Secretomotor fibre for parotid glands are in Otic ganglion
68. Anterior choroidal artery is a branch of internal carotid artery
69. Extra dural hematoma is caused by the bleeding from: ant division of middle meningeal artery
70. Patient right eye is deviated outward and downward, lesion is in oculomotor nerve
71. Inferior thyroid artery is related to recurrent laryngeal nerve
72. Superior thyroid vein drains into internal jugular vein
73. GVE fibres for lacrimal and nasal glands are in pterygopalatine ganglion
74. Which nerve doesn't pass through cavernous sinus : Mandibular nerve
75. Buccinator muscle is supplied by. Facial nerve
76. In cavernous sinus thrombus is due to Superior ophthalmic vein
77. Trigeminal ganglion is in middle cranial fossa
78. A boy came in Hosp with complains of loss of sensation over nose and mouth extending upto temporal region, nerve involve is maxillary division of trigeminal Nerve
79. Patient with tic doloreaux (Trigeminal neuralgia), analgesia given to block trigeminal ganglion at : Middle cranial fossa
80. The dorsal vagal nucleus is present in medulla oblongata
81. Intracranial and extracranial veins are joined by . Emissary Veins.
82. A male has enlarged posterior cervical Lymph nodes, while taking biopsy, which nerve can be damaged. → Spinal Accessory nerve
83. Subdural hematoma due to Bridging veins > rupture of superior cerebral vein.
84. Which nerve lies in the cavernous sinus? Abducent (prefer it due to its central location)
85. Profuse bleeding anterior to SCM : External Jugular vein involves
86. Bleeding posterior to SCM : 2 nd part of Subclavian artery
87. Foramen Ovale has Accessory Meningeal artery (Mnemonics = MALE)
88. Foramen Spinosum – Middle Meningeal artery passes
89. Superior Orbital Fissure – V1(Ophthalmic nerve) passes
90. Foramen Rotundum—V2(Maxillary Nerve) Pass
91. Foramen Ovale V3 (Mandibular Nerve) pass
92. Jugular Foramen – CN 9,10,11 (Accessory part), & Sigmoid Sinus
93. Hypoglossal Canal : has CN 12
94. Foramen Magnum : Brainstem + Spinal Part of CN11 is present.
95. Ansa Cervicalis root value is Hypoglossal with C1,2,3
96. Key Muscle of Neck or neck demarcation muscle is SCM > Scalene Anterior
97. Stylohyoid nerve supply is -- Facial nerve.
98. Sternohyoid and Sternothyroid nerve supply is -- Ansa cervicalis C1-3
99. Geniohyoid and Thyrohyoid nerve supply -- C1 through Hypoglossal nerve
100. Deep to posterior digastric and near palatoglossus a structure runs obliquely upwards is Lingual artery
101. Vertical artery runs obliquely upwards under submandibular gland is Facial artery
102. Mandibular nerve supplies Muscle of mastication, Tensor veli palatini ,Tensor veli tympani, Mylohyoid & Anterior belly of digastric
103. CN V motor lesion : Jaw deviates toward side of lesion
104. CN X lesion : Uvula deviates away from side of lesion
105. CN XI lesion: Weakness turning head to contralateral side of lesion (SCM) Shoulder droop on side of lesion (trapezius)
106. CN XII LMN lesion: Tongue deviates toward side of lesion

107. Vertical Diplopia : CN 4 > CN3
108. Diplopia on seeing down (vertical) & right and left (horizontal) : 3 rd nerve palsy
109.6 Nerve palsy- Diplopia on seeing right or left (horizontal)
110. Facial nerve enters temporal region Internal acoustic meatus
111. Facial Nerve Enters Posterior cranial Fossa + exits skull by Stylomastoid foramen
112. Facial nerve enters temporal region and exits posterior cranial fossa by Internal acoustic meatus
113. Facial Nerve exits Skull by Stylomastoid foramen
114. Facial Nerve normally causes closing of eye and Damage to Facial nerve result in Opening of Eye
115. Posterior 1/3 rd Tongue Lymph drains via - Jugulo omohyoid L.Ns
116. Tip of Tongue Lymph drainage – Submental nodes
117. Anterior 2/3 rd Taste sensation tongue – Chorda tympani
118. Posterior 1/3 rd Taste sensation – Glossopharyngeal nerve
119. Posterior most part of tongue Taste sensation by Vagus nerve
120. After thyroidectomy Loose Vocal Cord muscle involved is – Vocalis and Thyroarytenoid
121. After thyroidectomy Loose Vocal Cord muscle damage is -Cricothyroid
122. After thyroidectomy Tense Vocal Cord muscle involved is -Cricothyroid
123. After thyroidectomy Tense Vocal Cord muscle damage is -Vocalis and Thyroarytenoid
124. Abductor of Vocal cord or open Glottis : Posterior Cricothyroid
125. Close Glottis or Adductor of Vocal cord : Lateral and Transverse Cricothyroids > thyroarytenoids/Cricothyroid
126. Tense Vocal Cord : Cricothyroid → External laryngeal nerve
127. Relax Vocal Cord : Thyroarytenoids + Vocalis > Thyroarytenoid > Vocalis
128. Open Larynx Inlet : Thyro-epiglottic
129. Close Larynx Inlet : Aryepiglottic + Oblique arytenoids
130. Postganglionic fibres to Lacrimal gland via Maxillary nerve
131. General visceral efferent i.e., GVE : Supply smooth muscles and glands
132. Irritant solution snored , Which nerve carries that to brain → Trigeminal
133. Pituitary tumor invades anteriorly Optic nerve , superiorly Optic chiasma, laterally cavernous sinuses, inferiorly Sphenoid sinus , if Q is about Bone ? Pituitary tumor invades Sphenoid bone
134. Horizontal or medial nystagmus → Abducent nerve involved
135. Incisive foramen : has Nasopalatine nerve
136. Pt with diplopia , suddenly fell down can't reach phone → ACA infarct
137. To lower pitch of voice : Thyroarytenoid > Vocalis
138. If ICA is blocked , blood through Supra orbital artery can supply scalp
139. Geniohyoid : Elevates hyoid + depresses mandible or jaw
140. Lesion of hereditary telangiectasia → on Lips most commonly
141. All 4 PT glands are supplied by Inferior thyroid artery
142. Left RLN hooks around Ligamentum arteriosum > arch of aorta
143. Fracture of skull base with Loss of taste , vomiting → Jugular foramen lesion
144. Fracture of skull with facial paralysis and vertigo or hearing loss → internal acoustic meatus lesion
145. Mylohyoid muscle divides submandibular gland into 2 parts superficial and deep
146. Pt can't comb hairs → Spinal accessory nerve damaged (not cranial accessory)
147. Avoid local anaesthesia in penetrating eye injury
148. Hoarseness of voice + base of skull tumor → vagus nerve lesion
149. Max stability to TMJ by Temporo-mandibular ligament > Capsule of joint
150. TM ligament also prevents excessive Mouth opening
151. Lateral pterygoid prevents the joint to go back in cavity
152. Prevention of excessive medial and lateral movement of TMJ by Collateral ligaments
153. ELN is most common nerve to be injured in Thyroidectomy ; RLN in tracheostomy
154. Foramen caecum transmits Emissary veins
155. Mass in Ligamentum arteriosum can compress Left RLN
156. Trachea & RLN are Posterior to Arch of Aorta, or we can say Anterior to Trachea is the Arch of aorta.
157. Facial nerve supplies Lacrimal gland generally , post ganglionic to lacrimal via Maxillary nerve
158. Posterior auricular artery supplies external ear
159. Stenson's duct location is inside Buccal space

160.b/w superficial & deep parotid gland is Facial nerve(not parotid duct)
161.Mandibular nerve origin in oral cavity is Under Canine teeth a little below
162.Regarding Orbital injury, if Roof is damaged → Proptosis, If Floor is damaged → Enophthalmos.
163.Petrous part of temporal bone forms base of Middle cranial fossa
164.Medial palpebral ligament is attached to : Lacrimal ridges (ant + Post both)
165.PHRENIC Nerve is anterior to Scalene anterior muscle
166.Posterior surface of Superior PT glands is at level of 1 st tracheal ring
167.Fenestrations in choriocapillaris is maximum at SUB MACULAR area
168.Tympanic reflex dampens loud noises
169.Ganglion cells in retinal can : self-generate impulses
170.Spinal accessory nerve passes through SCM , not anterior
171.Lacrimal gland receives pre-ganglionic fibres from : Greater petrosal nerve
172.In posterior cervical lymphadenopathy : CN XI can be involved
173.Vesicle below clavicle and above sternum → C3/C4 lesion
174.If baby prefers feeder instead of breast feed → cleft SOFT PALATE (not Hard palate)
175.Infratemporal fossa is connected by Greater wing of sphenoid to temporal fossa
176.Sound is best perceived at Cochlear nucleus
177.If pt can't localize the direction of sound from where it is coming : Lateral Superior Olivary nucleus lesion > Medial geniculate body. Prefer Superior Olivary nucleus (Lateral)
178.If Eyeball moves upward + outward while closing eye is called BELL's phenomena
179.ICA is involved in Pituitary infarct , Not ACA, or MCA
180.SCM rotates head on contralateral side
181.Masseteric fascia develops from : Superficial layer of deep cervical fascia
182.Ptois , mydriasis + bilateral horizontal diplopia → CN III palsy
183.Posterolateral to thyroid gland is CAROTID sheath ; PG glands are posterior
184.Deep to carotid sheath lies Sympathetic trunk
185.Pharynx , larynx , trachea and RLN are Medial to thyroid gland
186.Strap muscles e.g., sternohyoid are anterior to thyroid gland
187.ANSA CERVICALIS supplies : Omohyoid , Sternohyoid & sternohyoid
188.Basilar artery is anterior to pons and supplies it
189.MELANOMA invades orbital cavity by EMISSARY Veins
190.Pleomorphic adenoma is slow growing Parotid tumor
191.Adenoid cystic carcinoma invades neural sheaths.
192.Falx cerebri prevents damage from rotatory head movements
193.Angle of mandible is mandibular bridge.
194.Pneumatic bones are more in Face (Not Skull)
195.Facial nerve supplies middle ear which walls : Medial and posterior walls
196.Maxillary artery supplies 1 st aortic arch
197.Inferior belly of OMOHYOID divides Posterior triangle
198.Superior belly of Omohyoid forms boundary of Carotid sheath
199.Injury to scalene anterior & 1 st rib with feeble distal pulses → subclavian artery lesion
200.Maxillary vein + Superficial temporal = retromandibular vein.
201.RMB + Post auricular vein = EJV
202.SUB mandibular + submental nodes are involved in cancer of : Lower Lip > Tongue
203.Pituitary gland lies BELOW diaphragm sella.
204.Digastric muscle is attached to Hyoid bone
205.RETROPHARYNGEAL NODES Drain : Pharynx + Eustachian tube
206.Optic nerve goes to skull via passing through opening in Ethmoid bone
207.B/w SCM , posterior digastric belly & Superior belly of Omohyoid → CAROTID Triangle is formed
208.IJV is lateral to ICA (artery is medially)
209.C4/C5 supplies levator scapulae
210.Sub occipital nerve supplies : Rectus capitis Posterior
211.Bleed from mastoid antrum Post wall → Sigmoid sinus involved
212.If Bleeding from Ant wall → ICA lesion

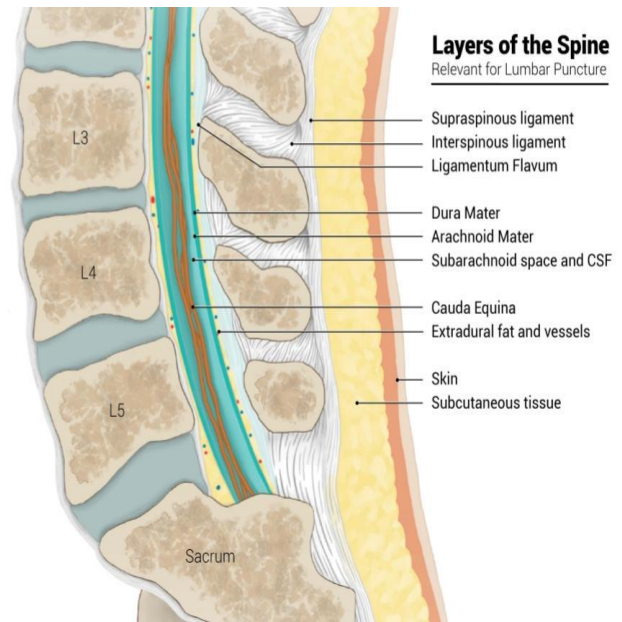
213.If Bleed is from FLOOR of Mastoid antrum → INT JUGULAR VEIN involved
214.Lesion at Rt optic radiations ,fibres in temporal lobe/Meyer's loop → Lt superior Quadrantanopia
215.If lesion of Parietal lobe fibres related to Optic radiations → inferior Quadrantopia
216.Pre-auricular or Parotid swelling + Otorrhea + Lymphadenopathy → TRUCUT BIOPSY is done
217.If just parotid swelling & no lymphadenopathy is there → FINE NEEDLE ASPIRATION (FNAC)
218.Child aspirated coin and presented with vomiting → RLN involved.
219.CHOROID MELANOMA is a Tumor of eye spreads to Liver.
220.Anterior division of middle meningeal artery is involved in Pterion fracture
221.HZV affects Facial nerve whereas HSV affects Trigeminal nerve commonly
222.Nerve supplying Medial pterygoid also supplies Tensor veli palatini
223.External nose is drained by Submandibular L.Ns
224.Immediate relation of IJV after exit from jugular foramen → ICA
225.But within foramina IJV related to CN 11.
226.Artery b/w trachea and sternohyoid → CCA, also on Upper border of thyroid cartilage - At C4 bifurcates.
227.Facial nerve is the most superficial in parotid gland
228.Broad nose , syndactyly and dished in appearance → Apert syndrome
229.Pituitary tumors may cause Junctional Scotomas
230.In Lt eye Light reflex or Pupillary reflex is present , but indirect or Consensual reflex is absent → Pretectum damaged
231.The sequence for this scenario is : pre tectum lesion > right optic nerve lesion > left oculomotor lesion
232.Indirect reflex will be absent in : Contralateral optic nerve damage + Pretectum + Ipsilateral parasympathetic fibre in oculomotor nerve
233.Direct reflex will be absent in lesion of ipsilateral optic nerve damage + Pretectum + Ipsilateral parasympathetic fibres travelling in oculomotor nerve
234.Middle ear is aerated by or receives air through anterior wall Via Eustachian Tube.
235.Air goes through Petrous temporal bone into Inner ear via Which wall of Middle Ear : Posterior wall
236.Composition of air in Middle ear is N 83% , O2 9% , CO2 6%

SPINE & SPINAL CORD

VERTEBRAL COLUMN		
Features	<p>Length : 71 Cm in Males (28 inch) and 61cm in Females (24 inches)</p> <p>33 Vertebrae:</p> <p>7cervical (atlas, axis & C7 are atypical), 12 thoracic, 5 lumbar, 5 sacral (fused) and 4 coccygeal (3-5)</p> <p>Features of a Typical Vertebrae:</p> <ul style="list-style-type: none"> ○ Body: anteriorly short cylindrical and rounded from Side to side. ○ Pedicles: present right and left, short and Rounded, project backward and laterally. ○ Pedicle is continuous, postero-medially with a Vertical plate of bone called Lamina. ○ Pedicle and Lamina constitute a Vertebral arch. ○ On side of pedicles and behind by Lamina -- large Vertebral Foramen present ○ Connection b/w body (centrum) and neural arch is by pedicle. ○ Most Medial Fibres of Erector Spinae muscle are attached to the Spinous processes of Vertebrae. 	
Functions	<p>Weight bearing, Movement of trunk, Support for limbs, Protection of spinal cord, Production of blood and Metabolic reserves (Calcium)</p> <ul style="list-style-type: none"> ○ Weight Bearing: ○ weight bearing line of Vertebrae pass through the Body of Vertebrae. Wt. bearing is: ○ Aided by secondary lordosis, 40% bony wedge , 60 %disc wedge. ○ caused/held by Extensor spinal muscles (supplied by Posterior Primary Rami of Spinal nerves) ○ Aided by intervertebral discs -- Dampeners, resilient, compressible ○ Intervertebral Discs: ○ Discs are the Notochord remnant and made of Fibrocartilage. ○ 15% of disc is Gelatinous, occasional cells, 90% water normally—70% in old age. ○ Increasing collagen with age and Decreasing elasticity with age ○ Joint b/w intervertebral discs are Secondary Cartilaginous joints 	
Movements	Region	Movements
	Cervical	Flexion , Extension , Lateral Flexion Movement of saying YES → Atlanto-Occipital joint (head nodding). Movement of saying NO → Atlanto-axial joints.
	Thoracic	Rotation only in unexplained Hypotension -- thoracic region must be examined
	Lumbar	Flexion, extension, and lateral flexion. No Rotation occurs.
	Sacral	No movement
	Coccygeal	No movement
Curvatures	<p>Lordosis is characterized by increase curvature of Vertebral Column = Convex Anteriorly</p> <p>In a Nutshell:</p> <ul style="list-style-type: none"> • Lordosis or Lordotic Curve(Cervical & Lumbar) = Concave Posteriorly means Convex Anteriorly • Kyphosis or Kyphotic Curve –(Thoracic & Sacral) = Concave Anteriorly means Convex Posteriorly • Scoliosis : Lateral or sideways deviations or curves of Spine (L in Lateral & scoliosis) • A Cobb's angle is a measure of spinal curvature and describes the maximum distance from straight a scoliotic curve may be. • Generally, it takes at least 10 degrees of deviation from straight before scoliosis is defined. 	
Ligaments	<p>Present throughout the vertebral column:</p> <ul style="list-style-type: none"> ○ Anterior and posterior longitudinal ligaments: Long ligaments that run the length of the vertebral column, covering the vertebral bodies and intervertebral discs. ○ Ligamentum flavum: Connects the laminae of adjacent vertebrae. ○ Interspinous ligament: Connects the spinous processes of adjacent vertebrae. ○ Supraspinous ligament: Connects the tips of adjacent spinous processes. ○ (Note: In the cervical spine, the interspinous and supraspinous ligaments thicken and combine to form the nuchal ligament). <p>Unique to lumbar spine:</p> <p>The lumbosacral joint (between L5 and S1 vertebrae) is strengthened by the fan shaped iliolumbar ligaments radiating from the transverse processes of the L5 vertebra to the ilia of the pelvis</p>	

Needle passes through following structures:

1. Skin
2. Fascia and fat
3. Supraspinous ligament
4. Interspinous ligament
5. Ligamentum flavum
6. Epidural space – **epidural needle stops here**
7. Dura matter
8. Arachnoid matter
9. Subarachnoid space – **CSF collects here.**



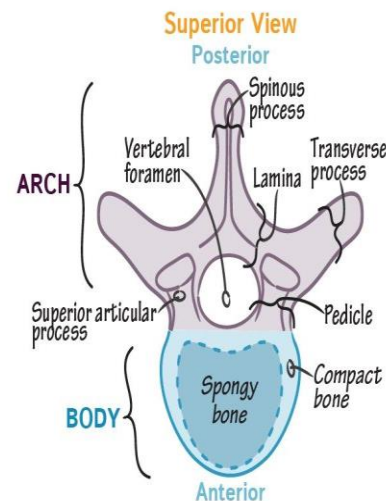
Blood supply

Spinal artery (Not Vertebral artery)

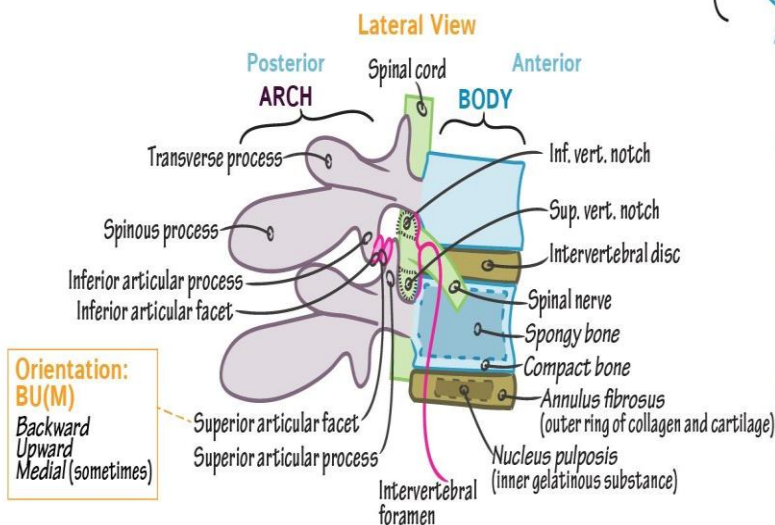


Vertebral Terminology

Anatomical **Embryological**
 Vertebral arch ~ Neural arch
 Vertebral body ~ Centrum
 Process: Bony prominence
 Spinous - 1
 Transverse - 2
 Articular - 4 (2 sup., 2 inf.)
 Articular facets (zygapophysial joints):
 Form at adjacent articular processes.



Cervical roots exit 1 above their corresponding vertebra, Thoracic roots and below, exit below it.



Orientation: BU(M)
 Backward
 Upward
 Medial (sometimes)

VERTEBRAE 33

Cervical (7)

Thoracic (12)

Lumbar (5)

Sacral (5 fused)

Coccygeal (3-4 fused)

SPINAL NERVES 31

Cervical (8)

Thoracic (12)

Lumbar (5)

Sacral (5)

Coccygeal (1)

<p>Cervical Vertebrae</p>	<p>There are eight (08) Cervical Somites, seven (07) Vertebrae & eight (08) Nerves (Remember --878)</p> <p><u>Imp Landmarks:</u> superior cervical ganglion at C1-C2, middle cervical ganglion -- C6, inferior cervical ganglion -- C7</p> <table border="1"> <tr> <td data-bbox="384 293 552 875"> <p>Atypical</p> </td><td data-bbox="552 293 1513 875"> <p>C1, C2, C7 Vertebrae are atypical cervical vertebrae.</p> <p><u>C1 (Atlas)</u></p> <ul style="list-style-type: none"> ❖ Lacks a body, no spinous process present, large triangular foramen transversum. ❖ Atlanto Occipital Joint is Biaxial Synovial Joint → movement of saying YES (flexion). <p><u>C2 (Axis)</u></p> <ul style="list-style-type: none"> ❖ has body and Dens / Odontoid process (it is fractured in Judicial Hanging) ❖ Atlanto Axial Joint Movement of saying NO Or Right & Left (Rotatory) <p><u>C7</u></p> <ul style="list-style-type: none"> ❖ No bifid Spine ❖ Vertebral artery doesn't pass from Foramen Transversum of C7 ❖ C7 develops from somites C7-C8 ❖ Cervical Rib arises from C7 vertebrae and compresses T1 Segment ❖ C7 Vertebra prominence has vestigial anterior tubercle, long non-bifid spinous process, and small foramen transversum containing vein only (no artery) ❖ Note that C7 nerve is Above C7 vertebra and C8 nerve is below it. </td></tr> <tr> <td data-bbox="384 875 552 1137"> <p>Typical</p> </td><td data-bbox="552 875 1513 1137"> <p>C3, C4, C5, C6 vertebrae. A typical vertebra has:</p> <ul style="list-style-type: none"> ❖ Bifid spinous process ❖ Large triangular foramen, short wide pedicle, and, small body ❖ Typical cervical vertebrae can be differentiated from thoracic by foramina Transversum. ❖ Foramen transversum has an Artery, a vein, sympathetic fibers from C6 to C1 ❖ C6 has enlarged anterior carotid tubercle of Chassaignac over which CCA passes. </td></tr> </table>	<p>Atypical</p>	<p>C1, C2, C7 Vertebrae are atypical cervical vertebrae.</p> <p><u>C1 (Atlas)</u></p> <ul style="list-style-type: none"> ❖ Lacks a body, no spinous process present, large triangular foramen transversum. ❖ Atlanto Occipital Joint is Biaxial Synovial Joint → movement of saying YES (flexion). <p><u>C2 (Axis)</u></p> <ul style="list-style-type: none"> ❖ has body and Dens / Odontoid process (it is fractured in Judicial Hanging) ❖ Atlanto Axial Joint Movement of saying NO Or Right & Left (Rotatory) <p><u>C7</u></p> <ul style="list-style-type: none"> ❖ No bifid Spine ❖ Vertebral artery doesn't pass from Foramen Transversum of C7 ❖ C7 develops from somites C7-C8 ❖ Cervical Rib arises from C7 vertebrae and compresses T1 Segment ❖ C7 Vertebra prominence has vestigial anterior tubercle, long non-bifid spinous process, and small foramen transversum containing vein only (no artery) ❖ Note that C7 nerve is Above C7 vertebra and C8 nerve is below it. 	<p>Typical</p>	<p>C3, C4, C5, C6 vertebrae. A typical vertebra has:</p> <ul style="list-style-type: none"> ❖ Bifid spinous process ❖ Large triangular foramen, short wide pedicle, and, small body ❖ Typical cervical vertebrae can be differentiated from thoracic by foramina Transversum. ❖ Foramen transversum has an Artery, a vein, sympathetic fibers from C6 to C1 ❖ C6 has enlarged anterior carotid tubercle of Chassaignac over which CCA passes.
<p>Atypical</p>	<p>C1, C2, C7 Vertebrae are atypical cervical vertebrae.</p> <p><u>C1 (Atlas)</u></p> <ul style="list-style-type: none"> ❖ Lacks a body, no spinous process present, large triangular foramen transversum. ❖ Atlanto Occipital Joint is Biaxial Synovial Joint → movement of saying YES (flexion). <p><u>C2 (Axis)</u></p> <ul style="list-style-type: none"> ❖ has body and Dens / Odontoid process (it is fractured in Judicial Hanging) ❖ Atlanto Axial Joint Movement of saying NO Or Right & Left (Rotatory) <p><u>C7</u></p> <ul style="list-style-type: none"> ❖ No bifid Spine ❖ Vertebral artery doesn't pass from Foramen Transversum of C7 ❖ C7 develops from somites C7-C8 ❖ Cervical Rib arises from C7 vertebrae and compresses T1 Segment ❖ C7 Vertebra prominence has vestigial anterior tubercle, long non-bifid spinous process, and small foramen transversum containing vein only (no artery) ❖ Note that C7 nerve is Above C7 vertebra and C8 nerve is below it. 				
<p>Typical</p>	<p>C3, C4, C5, C6 vertebrae. A typical vertebra has:</p> <ul style="list-style-type: none"> ❖ Bifid spinous process ❖ Large triangular foramen, short wide pedicle, and, small body ❖ Typical cervical vertebrae can be differentiated from thoracic by foramina Transversum. ❖ Foramen transversum has an Artery, a vein, sympathetic fibers from C6 to C1 ❖ C6 has enlarged anterior carotid tubercle of Chassaignac over which CCA passes. 				
<p>Thoracic Vertebrae</p>	<p><u>Features :</u></p> <ul style="list-style-type: none"> • Heart Shaped body (heart is in thorax) • Transverse processes project posteriorly at sharp angles. • Spinous processes are long and pointed and slope downward. • Bodies have facets on each side that articulate with ribs e.g., T2 articulates with Rib 2 & Rib 3 • From T3 vertebra, each vertebra Increases in size to bear the increasing load of body weight. • In unexplained Hypotension Thoracic region should be examined (due to major vessels in thorax). 				
<p>Lumbar Vertebrae</p>	<p><u>Features:</u></p> <ul style="list-style-type: none"> • Kidney shaped body (kidneys are in lumbar region) and triangular vertebral foramen. • Thick lamina and short spinous process • Superior articular surfaces face medially and inferior articular surface face laterally 				

KEY FACTS – VERTEBRAL COLUMN, LP AND SPINAL CORD	
❖	Ligament that supports odontoid process of axis on atlas = Transverse ligament
❖	Hanging causes death due to fracture of = odontoid process of axis > pedicle of C2 vertebra
❖	In forceful flexion of neck which ligament is torn = Ligamentum nuchae
❖	In hyperflexion, ligamentum nuchae damages first.
❖	In hyperextension, anterior longitudinal ligament is damaged
❖	Coccygeal ligament is extension of Dura mater and (Denticulate ligament is extension of Pia mater)
❖	Regarding denticulate ligament = It is adherent to arachnoid and dura matter
❖	Spinal cord suspended in dura by = Denticulate ligament
❖	Which structure keeps spinal cord in canal = denticulate ligament
❖	In lumbar puncture which structure is most likely damaged = Ligamentum Flavum
❖	Which space is accessed after piercing the inter laminar ligament during LP = Epidural space
❖	Epidural space contains venous plexus and Subarachnoid space has = CSF
❖	After LP patient complaints of headache this is most likely due to = dural stretch or stretch of falx cerebri
❖	Needle inserted at Para Median canal pierces = Ligamentum Flavum
❖	During LP Longitudinal Spinal Ligament is NOT Punctured
❖	The needle must pass through in Sequence Given below: Skin, subcutaneous fat, supraspinous ligament, interspinous ligament, and ligamentum flavum, Epidural space, Dura, Subarachnoid space. So, after Ligamentum Flavum, needle will be in Epidural space
❖	In Neonates, Spinal Cord ends at Lower border of L2 OR Upper L3
❖	In Adults, Spinal Cord ends at L1 (Lower border)
❖	Coccygeal segment of Spinal Cord is at L1 level
❖	Iliac crest is Palpable at the level of L4 (L4/L5)
❖	Best site for LP is above Spinous process of L4 but commonly LP is performed between L4/L5 > L3/L4
❖	Chordoma Involves Vertebrae (Not Spinal Cord)
❖	Spinal Cord ends at (Conus Medullaris) → lower L1 level in Adult and upper L3 in Children
❖	Filum terminale(internum) extension of pia matter, it ends at S2 level
❖	Dura matter ends at S2 level. Arachnoid matter ends at S2 level
❖	Coccygeal ligament is extension of dura matter (Filum terminale externum)
❖	It starts from S2 and ends at Coccyx

SPINAL CORD													
Features	<p>42-45 cm in length and 2.5 cm wide. Gray matter on the inside and White matter on the outside</p> <ul style="list-style-type: none"> ■ Gray matter is composed of neuron bodies Found in center of spinal cord and looks like a butterfly 3 Horns of Gray matter: Dorsal (sensory), ventral (motor) and intermedio-lateral horns (autonomic) ANS is present in T1 – L3 (intermediate horn) Clarke's column or Nucleus extends from. C8 – L2 > T1 - L2 ■ White matter is composed of axons covered in Myelin, it has tracts and fasciculi 3 columns of white matter : Posterior (DCML) anterior (spinothalamic tracts) and lateral (Corticospinal tract). These are called funiculi (large group of axons). ■ Two enlargements of Spinal Cord are: <ol style="list-style-type: none"> 1. Cervical enlargement (C5 -T1, Brachial Plexus) supply upper Limbs , rarely C4 and T2 contribute 2. Lumbar enlargement (L2-S3) supply lower Limbs via Lumbosacral Plexus ■ Conus medullaris (inferior end): Spinal cord tapers off to end at L1 in adults and L3 in children ■ Filum terminale (internum) is pia mater extension that anchors cord to Coccyx ■ Cauda equina (horse tail) nerves below L2 <p>It consists of 4 pairs of lower Lumbar , 5 sacral pairs , 1 coccygeal pair.</p> <ul style="list-style-type: none"> ■ Denticulate ligaments suspend cord in dural sheath ■ Filum terminale Externum/Coccygeal ligament is extension of Dura mater and (Denticulate ligament is extension of Pia mater).Starts from S2 and ends at Coccyx denticulate ligament Is adherent to arachnoid and dura matter. ■ There are 31 pairs of spinal nerves Each spinal segment gives rise to one Spinal nerve pair. <p>C1-C7 spinal nerves project ABOVE C1-C7 Vertebrae.C8 spinal nerve projects below C7 vertebra</p> <p>Vertebral Venous Plexus is Present in Epidural Space</p> <ul style="list-style-type: none"> ■ CSF +Major vessels (radicular,segmental,medullary,spinal arteries are present in Subarachnoid Space ■ Dura & Subarachnoid space ends at S2 or S2/S3. Pia matter extends upto Tip of Coccyx ■ Dural Venous Sinuses are present in Sub Dural Space 												
Rexed Laminae	<ul style="list-style-type: none"> • Anterior or Ventral Horn -- Lamina 8 & 9 • Posterior or Dorsal Horn -- Lamina 1 to 6 • Lamina 7 &10 -- Intermediate Horn 												
Total (10)	<table> <tr> <td>Lamina 1</td><td>High Threshold mechanoreceptor, Noxious stimulus & A delta pain fibres</td></tr> <tr> <td>Lamina 2</td><td>C fiber & Substantia gelatinosa (slow Pain)</td></tr> <tr> <td>Lamina 3,4</td><td>Low Threshold mechanoreceptor</td></tr> <tr> <td>Lamina 6</td><td>Deepest Layer, Joint skin Signal and proprioception</td></tr> <tr> <td>Lamina 7</td><td>Largest Area, Dorsal Nucleus of Clarke – Spinocerebellar pathway</td></tr> <tr> <td>Lamina 10</td><td>Central canal</td></tr> </table>	Lamina 1	High Threshold mechanoreceptor, Noxious stimulus & A delta pain fibres	Lamina 2	C fiber & Substantia gelatinosa (slow Pain)	Lamina 3,4	Low Threshold mechanoreceptor	Lamina 6	Deepest Layer, Joint skin Signal and proprioception	Lamina 7	Largest Area, Dorsal Nucleus of Clarke – Spinocerebellar pathway	Lamina 10	Central canal
Lamina 1	High Threshold mechanoreceptor, Noxious stimulus & A delta pain fibres												
Lamina 2	C fiber & Substantia gelatinosa (slow Pain)												
Lamina 3,4	Low Threshold mechanoreceptor												
Lamina 6	Deepest Layer, Joint skin Signal and proprioception												
Lamina 7	Largest Area, Dorsal Nucleus of Clarke – Spinocerebellar pathway												
Lamina 10	Central canal												
Blood Supply	<p>Spinal Artery (Branch of Vertebral Artery)</p> <ul style="list-style-type: none"> ○ Primary Blood Supply of Anterior 2/3rd of Spinal Cord Is by Anterior Spinal Artery ○ Posterior 1/3rd of cord is supplied by Posterior Spinal Artery 												
Clinical anatomy	<ul style="list-style-type: none"> ○ Polio involves anterior horn and Damage LMN ○ Syringomyelia may present with hydrocephalus and Arnold-Chiari I malformation. ○ Syringomyelia results in a "belt-like" or "cape-like" loss of pain and temperature bilaterally. ○ Loss of Contralateral Temperature and Intact Pain sensation lesion of – Dorsal root S1 involved. ○ Spina Bifida: ○ A type of Neural tube defects due to Folic acid deficiency in Pregnancy , DM, Obesity with some unknown factors or drugs. ○ Folic acid 400mcg must be given to all pregnant daily. ○ Types : Main 3 types are as follows: ○ Spina Bifida Occulta is the most common but least dangerous. ○ a tuft of hair seen at the back of child. AFP is normal. 												

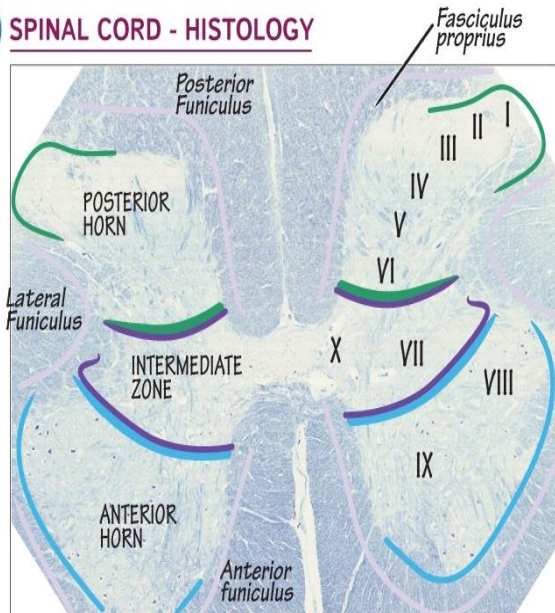
- **Meningocele** -- opening at the back or herniated sac contains only Meninges.
- **Meningomyelocele** sac contains Neural tissues + meninges -- most dangerous type
- Diagnosis :**
- Early diagnosis by **USG** > Amniocentesis or AFP.
- AFP is raised in All types except Spina bifida Occulta

Relationship of Spinal cord segments to Vertebral numbers

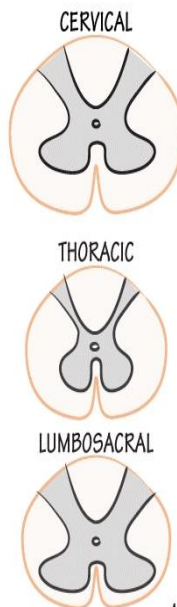
Because spinal cord is shorter than vertebral column, the spinal cord segments do not correspond numerically with the vertebrae that lie at same level. The following list helps to determine which spinal segment lies at vertebral level.

VERTEBRAE	SPINAL SEGMENT
Cervical	Add 1
Upper thoracic	Add 2
Lower thoracic (T7-T9)	Add 3
Tenth thoracic (T10)	L1 and L2 spinal cord segments
Eleventh thoracic (T11)	L3 and L3 spinal cord segments
Twelfth thoracic (T12)	L5 spinal cord segment
First Lumbar (L1)	Sacral and coccygeal spinal cord segments

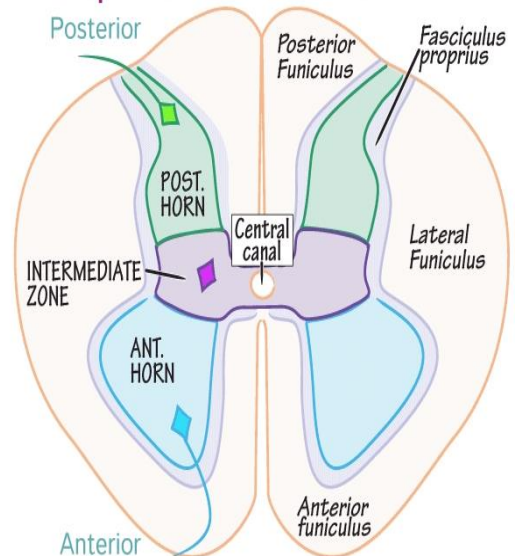
SPINAL CORD - HISTOLOGY



Rostro-Caudal Levels



Spinal Cord: Axial Cross-Section



Key Structures

WHITE MATTER FUNICULI

- Posterior - Large, Proprioceptive afferents
- Lateral - Large, Motor efferents
- Anterior - Small, Thermo/nociceptive afferents

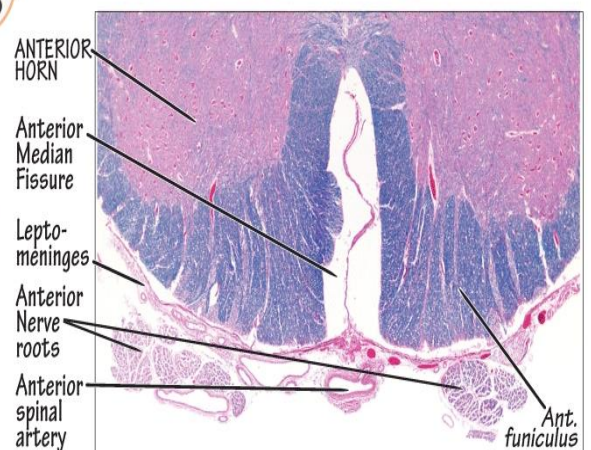
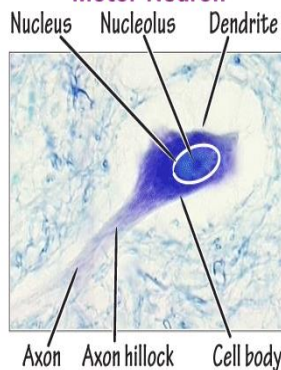
GRAY MATTER

- Posterior horn - Sensory nuclei
- Intermediate zone - Autonomic & Spinocerebellar n.
- Anterior horn - Motor nuclei

NOTABLE REXED LAMINAE

- Lamina I - Marginal nucleus
- Lamina II - Substantia gelatinosa
- Laminae III & IV - Nucleus proprius
- Lamina VII - Dorsal N. Clarke, Intermediolateral cell column

Motor Neuron



PATHWAYS OR TRACTS OF SPINAL CORD

ASCENDING TRACTS (SENSORY)

- Spinothalamic tract -- STT (Anterior and Lateral Spinothalamic tract)
 - Dorsal Column -- Medial Lemniscus system (Fasciculus cuneatus and gracillus)
 - Spinocerebellar pathways (Anterior/ventral and posterior/dorsal spinocerebellar)
 - Others: Spinotectal tract, Spinoreticular tract and spino olivary tract
- Features:**
- 1st Order neurons Originate for Spinothalamic + DCML → From Posterior or Dorsal Root Ganglion (DRG)
 - 2nd Order neurons origin: Spinothalamic tract + Substantia gelatinosa from DCML (Fasciculus Gracillus & Cuneatus)
 - 3rd Order Neurons origin for both STT & DCML → Ventral postero lateral nucleus of Thalamus (VPL Thalamus)
 - Sensations from Face travel via Trigeminothalamic pathway to VPM nucleus (also includes taste sensations)

Anterolateral Spinothalamic tract	<ul style="list-style-type: none"> • The anterior ST tract carry : Crud touch , itch & tickle. • Lateral tract carry Pain and Temperature. • Trigeminothalamic Tract carry Pain and Temperature from Face • Lesion of Lateral tract cause loss of contralateral pain + temp 1 or 2 segment below level of lesion. A-delta and C or class III and class IV dorsal root fibers are used in these pathways.
Dorsal Column Medial lemniscus system(DCML)	<ul style="list-style-type: none"> • It carries proprioception, vibration sense and fine touch and Two-point Discrimination • Class II or A-beta dorsal root fibers are present • Fasciculus Gracillus is Located in all spinal level Related to Lower limb • The fasciculus cuneatus at upper thoracic + cervical spinal cord levels - Related to Upper limb • Lesions of the dorsal columns result in a loss of joint position sensation, vibration, pressure critical touch and 2-point discrimination sensations. • There is loss of the ability to identify the characteristics of an object, called astereognosis (e.g size, Consistency, form, and shape), using only the sense of touch . • It is Evaluated by testing vibratory sense using a 128-Hz tuning fork. • Asking the patients to place their feet together if the patient sways with the eyes closed, this is a +Ve Romberg sign, indicates DCML lesion vs Fall with Open eye indicates cerebellar lesion • Astereognosis is due to lesion in Somaesthetic association area > Primary somatosensory area • In DCML Lesion : Sensory Ataxia > Astereognosis occurs.
Spinocerebellar pathway For Movement + positioning	<ul style="list-style-type: none"> • Dorsal spinocerebellar tract carries input from the lower extremities and lower trunk • Cuneo cerebellar tract carries input from the upper extremities and upper trunk • External posterior arcuate fibres form Cuneo cerebellar • External Anterior arcuate form Pontocerebellar • Internal arcuate form Dorsal column medial lemniscus pathway • Friedreich ataxia may affect these tract and Ataxic gait is the common symptom
Other Ascending pathways	<p>Spinotectal: brings about movements of eyes and head towards the source of stimulation</p> <p>Spinoreticular: mediates deep and chronic pain</p> <p>Spino-olivary: sends information to cerebellum from cutaneous and proprioceptive organs</p>

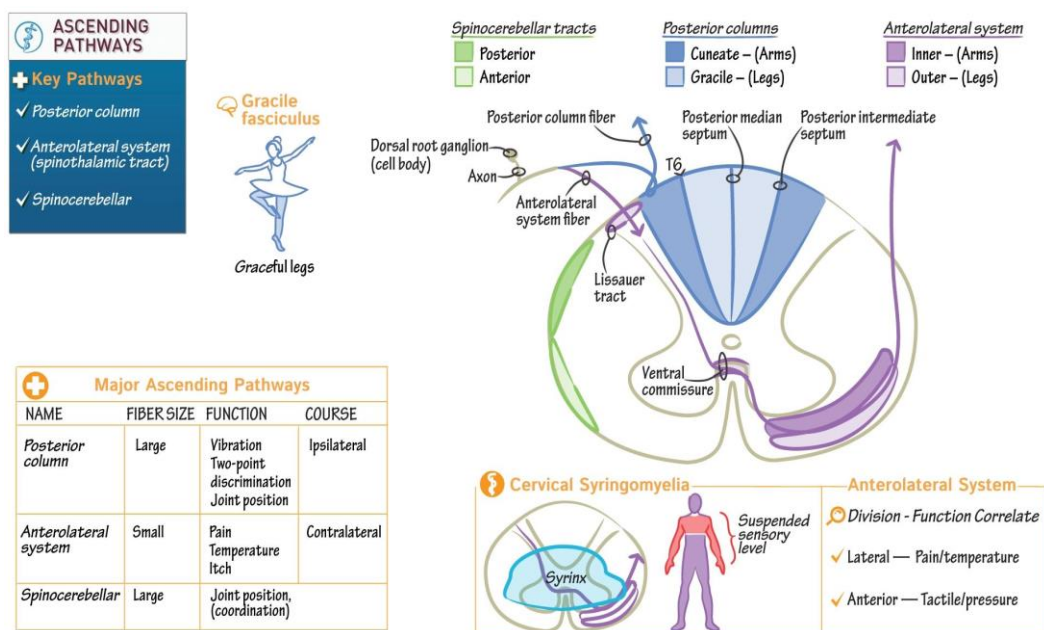
DESCENDING TRACTS (MOTOR)

- Corticospinal Tract or Pyramidal Tract (Anterior CST & Lateral CST)
- Extra pyramidal tracts: Rubrospinal, Vestibulospinal, Reticulospinal, Tectospinal and Medial Longitudinal fasciculus

Corticospinal tract(CST)	Lateral CST (Pyramidal tract)	Anterior CST
	<ul style="list-style-type: none"> ▪ Origin: from motor and premotor cortex ▪ Ends at motor neurons of ant gray column ▪ location in cord: lateral column ▪ 80-90% decussates in pyramid of medulla ▪ Carries out fine motor function of distal musculature e.g fine discrete movement of painter's hand ▪ If lesion of the corticospinal tract is above the pyramidal decussation, 	<ul style="list-style-type: none"> ▪ Origin: from motor and premotor cortex ▪ Ends at motor neurons of ant gray column ▪ location in cord: Anterior column ▪ Decussates after descending of fibers ▪ Controls gross and postural motor functions of axial + proximal musculature

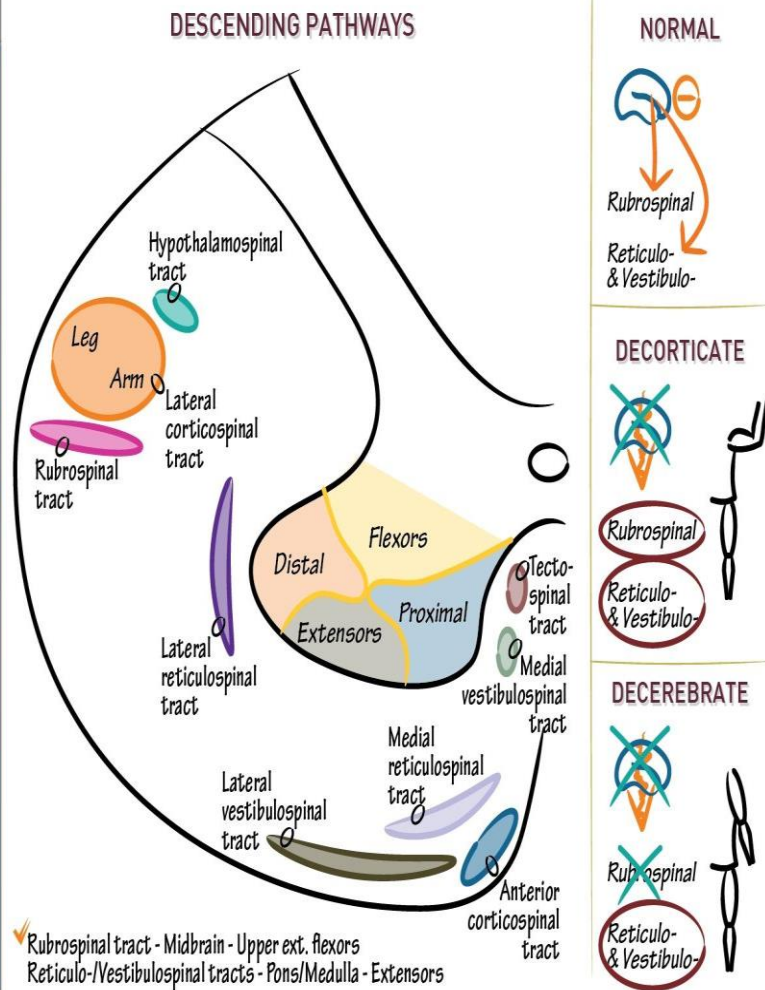
	<p>a weakness is seen in muscles on the contralateral side of body</p> <ul style="list-style-type: none"> If Lesions occur below this level, an ipsilateral muscle weakness is seen. 	
Extrapyramidal tracts	<ul style="list-style-type: none"> ➤ Rubrospinal: Facilitates the action of flexor muscles and inhibits the activity of extensors. ➤ Vestibulospinal: Facilitates the action of Extensor muscles, postural reflexes, and balance ➤ Reticulospinal: Modulates spinal reflexes and sensory transmission (especially pain) ➤ Tectospinal: Reflex head turning and reflex postural movement in response to visual stimuli. ➤ Medial longitudinal fasciculus: Co-ordination of head and eye movements ➤ Descending autonomic fibers: Modulate the autonomic functions 	

Hemisection of Spinal cord	<p>Also known as Brown-Sequard syndrome</p> <p>Ipsilateral Loss:</p> <ul style="list-style-type: none"> Ipsilateral loss of all sensation at level of lesion Ipsilateral LMN signs (eg, flaccid paralysis) at level of lesion Ipsilateral UMN signs below level of lesion (due to corticospinal tract damage) Ipsilateral loss of proprioception, vibration, light (2-point discrimination) touch, and tactile sense Below the level of lesion (due to dorsal column damage) <p>Contralateral Loss:</p> <p>Contralateral loss of pain, temperature, and crude (non-discriminative) touch below the level of lesion (due to spinothalamic tract damage)</p>
Bladder Injuries	<ul style="list-style-type: none"> Injury above sacral segment (sympathetic damage) causes: Spastic Bladder, Automatic Bladder & Urge Incontinence Injury At sacral segment (parasympathetic damage) causes: Atonic , Autonomous Bladder and Overflow Incontinence Neurogenic bladder is a common term for both spastic and Atonic Bladder.



+ DESCENDING PATHWAYS			
TRACT	ORIGIN	TERMINATION	FUNCTION
✓ LATERAL CORTICOSPINAL TRACT	Motor cortices (mostly)	Contralateral	Distal muscle activation
✓ ANTERIOR CORTICOSPINAL TRACT	Motor cortices (mostly)	Contralateral	Proximal muscle activation
✓ HYPOTHALAMO-SPINAL TRACT	Hypothalamus	Ipsilateral	Autonomic function
✓ RUBROSPINAL TRACT	Red nucleus	Contralateral	Activates upper limb flexion
✓ TECTO-SPINAL TRACT	Superior colliculus	Contralateral	Neck movement/ head turn
✓ MEDIAL RETICULOSPINAL TRACT	Pontine reticular formation	Ipsilateral (mostly)	Activates limb extension
✓ LATERAL RETICULOSPINAL TRACT	Medullary reticular formation	Bilateral*	Inhibits limb extension
✓ MEDIAL VESTIBULOSPINAL TRACT	Medial & spinal vestibular nuclei	Bilateral	Activates neck extensors
✓ LATERAL VESTIBULOSPINAL TRACT	Lateral vestibular nucleus	Ipsilateral	Activates para-vertebral & proximal limb extensors

*Intertextual discrepancy exists regarding the laterality of this pathway.



SPINAL NERVES

- There are 31 pairs of spinal nerves in total : 8 cervical , 12 thoracic , Lumbar 5 , Sacral 5 , 1 coccygeal
- Spinal nerves connect the CNS to sensory Receptors, muscles, and glands and are part of The peripheral nervous system. After emerging from intervertebral foramen Spinal nerve divides into :
 - Dorsal ramus : supplies skin and muscles of back
 - Ventral ramus : supplies skin and muscles of front of trunk and Upper and lower limbs
- Meningeal branch: supplies vertebrae, ligaments, meninges
- Ramus communicants : communicates with Autonomic nervous system
- Anterior and posterior roots attach a spinal Nerve to a segment
- C8 spinal nerve exits below C7 and above T1.
- Nerves C1-C7 exit above the corresponding vertebrae
- All other nerves exit below the corresponding vertebrae e.g C3 exits above the 3rd cervical vertebra; L2 below L2 V

Frequently Tested Concept in Exams

1. Nerve root present between L4-L5 is : L4
2. Disc herniation at L4-L5 , Compressed nerve root? L5 (exception ! explained below)
3. Nerve root b/w T4-T5 is T4 and in disc herniation of T4/T5 → T4 is compressed

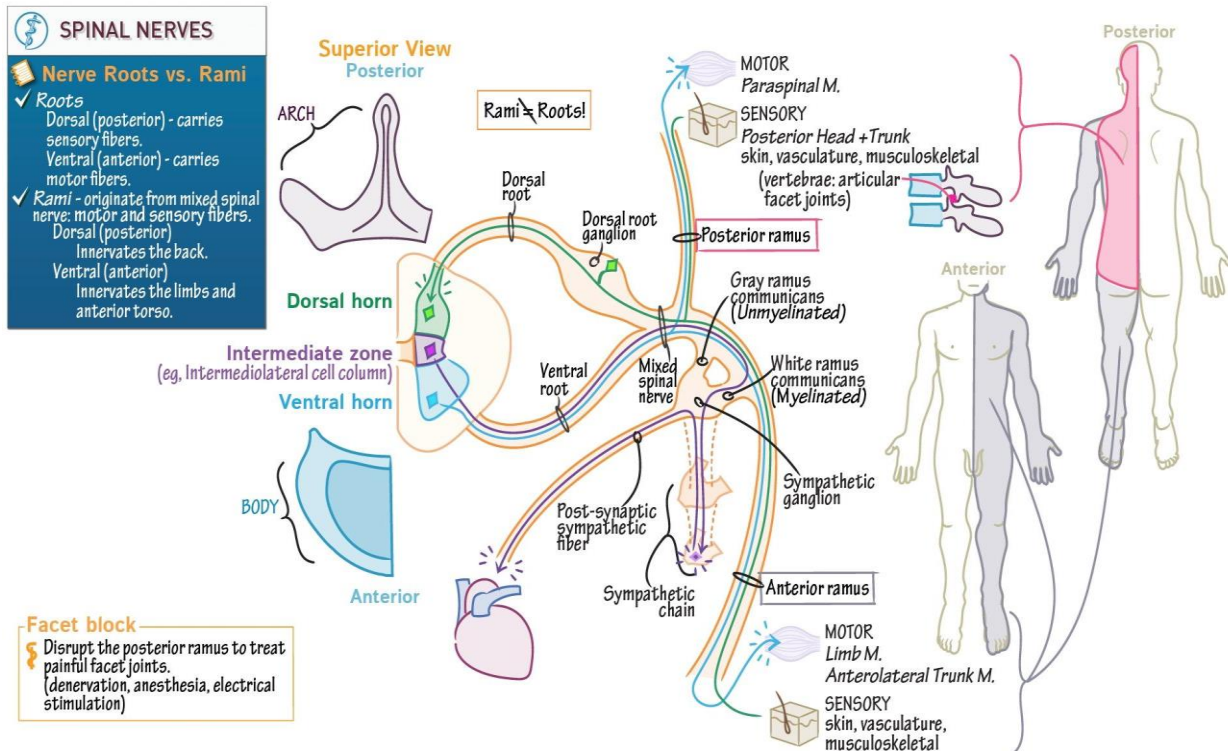
- Nerve present b/w C5/C6 vertebrae is → C6 nerve
- Nerve root compressed in disc herniation b/w. C5/C6 → C6

Explanation

The thoracic and lumbar roots exit below the vertebra of the corresponding number e.g from L4-L5 , 4th lumbar nerve root will arise. Because the nerve roots move laterally as they pass toward their exit, the root corresponding to that disc space (L4 in the case of the L4 to 5 disc) is already too lateral to be pressed on by the herniated disc.

Herniation of the L4 to L5 disc usually gives rise to symptoms referable to the L5 nerve roots, even though the L5 root exits between L5 and S1 vertebrae.

C1 – C7 roots project above vertebrae , C8 passes below C7 vertebrae



MENINGES

- Three layered Covering of Brain and Spinal Cord Consisting of Dura, Arachnoid and Pia Matter
- Leptomeninges = Arachnoid + Pia Matter.
- Pia matter covers the Sulci and Gyri of brain & extends till tip of coccyx.
- Dura and Arachnoid matter end at S2 .
- CSF is drained in Subarachnoid space and absorption of CSF is via Arachnoid granulations.

DURA MATTER

Layers of dura

- It consists of Outer endosteal (periosteal) and Inner meningeal (fibrous) layer (folds for Tentorium Cerebelli & Falx Cerebri.
- Outside both are present the middle meningeal vessels present (site of extra-dural Haemorrhage). Between the layers venous sinuses and Meckel's cave present
- Under both layers is the site for subdural haemorrhage (Bridging Veins > Superior Cerebral V)
- Subdural hematoma has Crescent shape on CT brain
- Extradural Hemorrhage occurs in Extra Dural Space b/w dura & Calvaria
- It has a lucid interval and appears lentiform Biconvex shaped on CT brain

DURAL PARTITIONS

Falx cerebri	<ul style="list-style-type: none"> The falx cerebri is a crescent-shaped structure that projects downwards between the two Cerebral hemispheres from the dura covering the calvaria or bone It is attached anteriorly to the crista Galli of the ethmoid bone and frontal crest of the frontal bone. Posteriorly it is attached to and blends with the tentorium cerebelli.
Tentorium cerebelli	<ul style="list-style-type: none"> A horizontal projection of the meningeal dura mater that covers and separates the cerebellum in the posterior cranial fossa from the posterior parts of the Cerebral hemispheres
Falx cerebelli	<ul style="list-style-type: none"> A small midline projection of meningeal dura mater in the posterior Cranial fossa. It is attached posteriorly to the internal occipital crest of the occipital bone and Superiorly to the tentorium cerebelli. Its anterior edge is free and is between the two Cerebellar hemispheres.
Diaphragma sellae	<ul style="list-style-type: none"> The final dural projection is the diaphragma sellae. This small horizontal shelf of meningeal Dura mater covers the hypophyseal fossa in the sella turcica of the sphenoid bone
Blood supply	<ul style="list-style-type: none"> via Middle meningeal artery, meningeal branches of vertebral, ophthalmic, Anterior ethmoidal, internal carotid and accessory meningeal artery
Nerve supply	<ul style="list-style-type: none"> Main nerve supply is via Trigeminal Nerve. In Anterior Cranial Fossa: Anterior ethmoidal (V1 branch) supplies dura In Middle Cranial fossa: Nervus spinosus (V3) and Middle meningeal nerve (branch of V2) In Posterior cranial fossa: Meningeal branches of glossopharyngeal (IX) and Vagus (X) nerve In Foramen magnum: C1-3 supplies dura Supratentorial supply via Meningeal branches from V1

SPINAL MENINGES

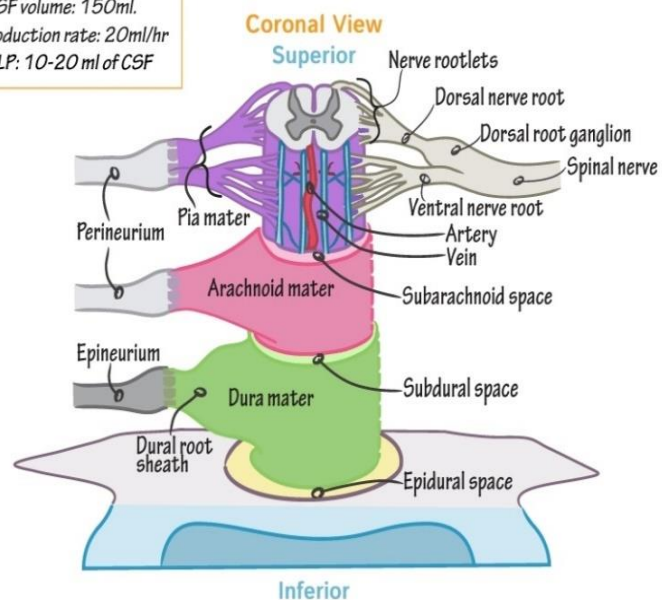
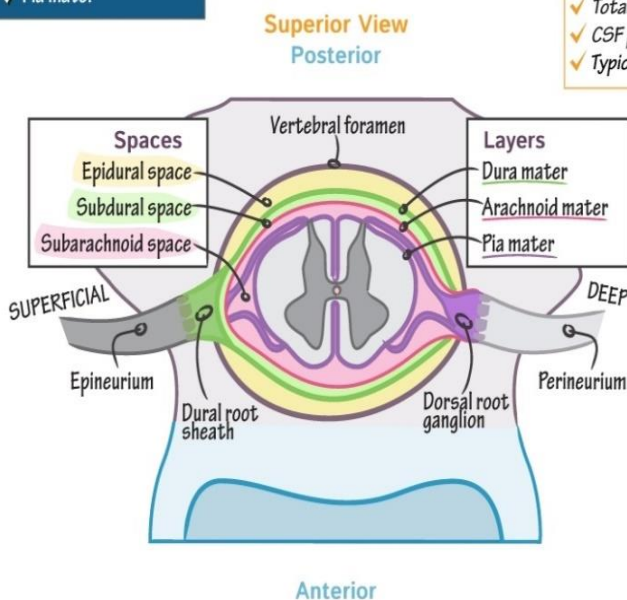
+ Meninges

- Epidural space
- ✓ Dura mater
- Subdural space
- ✓ Arachnoid mater
- Subarachnoid space
- ✓ Pia mater

Meningeal space	Space	Cranium Typical disease site?	Spine Space	Typical disease site?
Epidural	Potential	No (unless middle meningeal artery rupture or traumatic defect)	Actual	Yes (hematoma, infection, neoplasia)
Subdural	Potential	Yes (hematoma b/c of bridging veins)	Potential	No (NO dural sinuses, so NO bridging veins)
Subarachnoid	Actual	Yes (eg, hemorrhage, infection)	Actual	Yes (continuous w/cranium)

Lumbar Puncture

- ✓ Total CSF volume: 150ml.
- ✓ CSF production rate: 20ml/hr
- ✓ Typical LP: 10-20 ml of CSF



DURAL VENOUS SINUSES OR CRANIAL SINUSES		
Location	Between the two layers of the dura mater.	
Functions	To receive blood from the Brain, meninges, orbit, internal ear and Diploe. To collect CSF from the subarachnoid Space through the arachnoid villi. Ultimate destination is the Internal Jugular veins.	
Characteristics	Thickened wall -- lined by endothelium and devoid of any muscular tissue They are Valveless and connected to valveless emissary Veins.	
Paired sinuses	seven paired sinuses as follows: Transverse, cavernous, greater & lesser petrosal, sphenoparietal, sigmoid and basilar sinuses)	
Unpaired sinuses	Five unpaired, they include: Superior and inferior sagittal, straight sinus, occipital and intercavernous dural sinuses	
Summary of dural sinuses	Main drainage of blood in between cerebral circulation till internal jugular vein	
	Superior Sagittal Sinus	present in Vertex and reaches down till the confluence of sinuses (Straight Sinus). All dural sinuses will come to the confluence of sinuses. <u>Injury to vertex – superior sagittal sinus involved</u>
	Inferior Sagittal Sinus	ISS will come to straight sinus
	Cavernous sinus	Receiving from Sphenoparietal sinus, Superior ophthalmic vein, Inferior and superior petrosal sinus, Facial vein and Emissary veins
	Transverse sinuses	Lies Beneath Tentorium cerebelli. It Drains from : Left transverse sinus: Straight sinus Right transverse sinus: Superior sagittal sinus Transverse sinuses drains to Sigmoid sinus Drainage area: Base of telencephalon, cerebellum
	Straight Sinus	<u>Inferior Sagittal Sinus + Vein of Galen join to form straight sinus</u> It traverses the junction between falx cerebri and tentorium cerebelli
	Route to IJV	From confluence of sinus goes to: transverse sinus → sigmoid sinus →end of sigmoid → Internal Jugular Vein IJV = Sigmoid Sinus + Inferior Petrosal Sinus

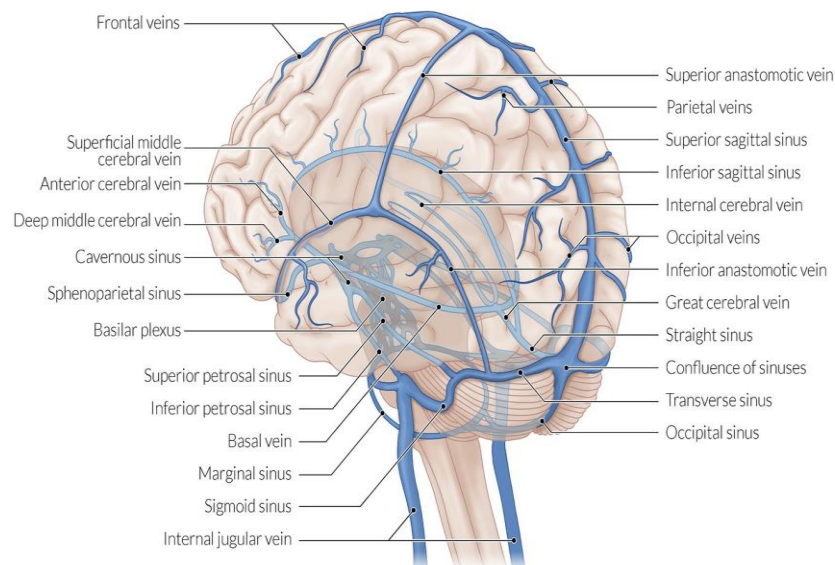
Cavernous Sinus

- Each lies alongside the body of the sphenoid in the middle cranial fossa between the periosteal (endosteal) and meningeal (fibrous) layers of dura.
- Roof: Anterior and posterior clinoid processes with uncus of temporal lobe + Int carotid artery on it, CN 3,4 into it.
- Lateral wall: Dura, temporal lobe, II, IV, V1, V2 in the wall
- Floor: Greater wing of sphenoid
- Medial wall: Dura over sphenoid, sella turcica, pituitary, sphenoid sinus
- Posterior wall: (narrow), dura of posterior fossa, superior and inferior Petrosal sinuses, peduncle of brain
- Anterior wall: (narrow), medial end of superior orbital fissure, Ophthalmic veins, orbit
- Contains: Internal carotid artery, CN VI & CN 3, 4
- Draining into it: Superior/inferior ophthalmic veins, intercavernous sinuses, sphenoparietal sinuses, superficial middle cerebral vein
- Draining out of it: Superior/inferior petrosal sinuses, emissary veins to Pterygoid plexus
- **Mnemonics For Contents – O TOM CAT**
Oculomotor nerve, Trochlear nerve, Ophthalmic nerve V1, Maxillary nerve V2, Carotid artery (ICA), Abducent Nerve Abducent Nerve is mostly damaged in cavernous sinus thrombosis due to central location.

VENOUS DRAINAGE OF BRAIN

- Great Cerebral Vein of Galen is formed by two internal cerebral veins.
- Thalamostriatal + Anterior septal veins drain into Internal Cerebral veins.
- Basal Vein is formed by anterior Cerebral vein + Deep Middle cerebral vein + inferior striate veins.
- Superficial Middle Cerebral vein drains the Lateral hemispheres and goes into cavernous sinus.
- Deep Middle Cerebral Vein : drains Insula, joined by Anterior cerebral and striate veins to forms Basal Vein.
- Basal Vein joins the Great Cerebral vein, which in turn drains into Straight Sinus.
- Superior Cerebral Vein : drains the Superolateral hemispheres. It empties into Superior Sagittal Sinus. Superiorly it can drain to the superficial middle cerebral vein. Laterally they drain via the superior and inferior petrosal veins to the sigmoid.
- **Dangerous Area of face:** by superior ophthalmic > inferior ophthalmic vein will Go to the cavernous sinus.
Deep facial vein goes to Pterygoid plexus vein is one of the dangerous Area.
Pterygoid plexus veins are connecting to Intra cranium by emissary veins.
Emissary vein from outside of pterygoid plexus till inside cavernous sinuses.

Cerebral Vein Thrombosis		
Risk Factors	Clinical Features	Diagnosis
Head injury Infection Tumors Pregnancy OCPs pro-thrombotic conditions	Venous congestion and obstruction leads to swelling and edema. Headache, seizures, motor deficits, encephalopathy, CN palsies CN palsies are associated with cavernous sinus, transverse sinus and IJV thrombosis	1 st line – MRI/MRV 2 nd line – CT Venography On contrast CT – Empty delta sign On non-contrast CT – delta sign



CEREBROSPINAL FLUID

- CSF Pressure = 10-20 cm H₂O or 60-150mm H₂O or 6-15mmhg.
- CSF production = 450-500 mL/day. 80 % CSF is in Subarachnoid space , Rest 20 % in Ventricles.
- CSF in Ventricle – 150ml ,formation at the rate of 20 ml/hr.
- CSF Density is 1.0005 & CSF Specific Gravity is 1.005.
- CSF PH is 7.33.CSF is isotonic with serum, has Equal sodium as compared to plasma.
- CSF has High magnesium and chloride and Creatinine as compared to plasma.
- Rest everything is Low in CSF as compared to plasma (Protein even Lower than glucose).
- CSF is produced by Ependymal cells (no basement membrane).
- Maximum determinant of CSF composition is Ependymal cells.
- CSF Provides nutrition to CNS and has Cushion like effect.
- Arachnoid granulations are seen by naked eye.
- Indicator for CSF Leak Beta 2 Transferrin.

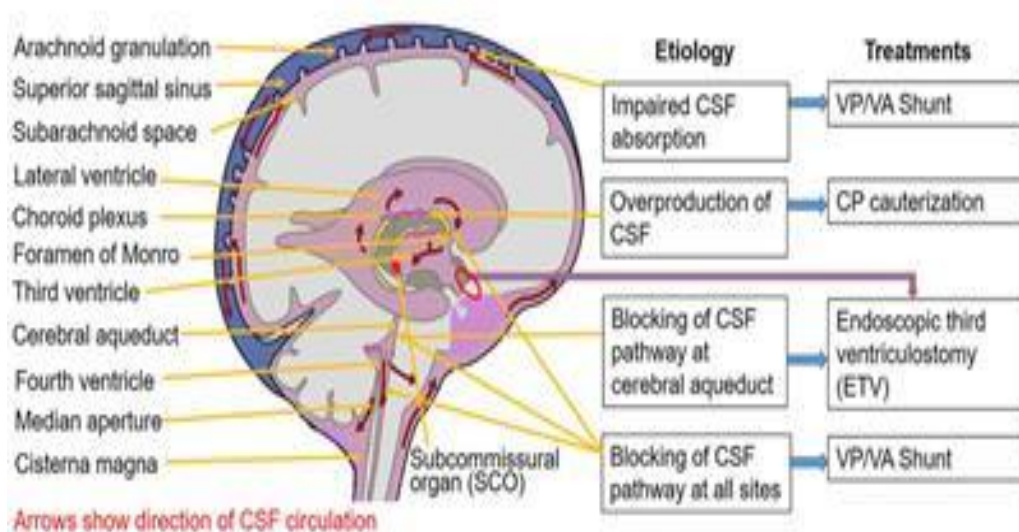
FLOW OF CSF

- Lateral ventricle to 3rd via Interventricular Foramina of Monro.
- 3rd to 4th via cerebral aqueduct (blockage can cause hydrocephalus).
- 4th to Subarachnoid space via Foramen Magendie and Foramen Luschka.
- CSF made by choroid plexus (Ependymal cells) in 4th and lateral ventricle.
- CSF absorbed by arachnoid granulations and then drains into Dural venous sinus.

Communicating, Obstructive and Normal pressure Hydrocephalus

- **Communicating Hydrocephalus** (Non-Obstructive) All 4 ventricles are enlarged
Causes: IVH of prematurity (grade III/IV), adult IVH, aneurysmal SAH, Meningitis. May do lumbar puncture
- **Obstructive Hydrocephalus** : Dilatation of lateral and 3rd ventricles with small/compressed/Normal 4th ventricle
- Asymmetry or enlargement of lateral ventricle when obstruction is at Foramen of Monro (e.g colloid cyst)
- Posterior fossa mass lesions (tumor, ICH, cyst), intraventricular mass, Lesions (tumor, IVH, cyst), aqueductal stenosis
- Do NOT do lumbar puncture in Obstructive or Non communicating Hydrocephalus
- **Normal Pressure Hydrocephalus** is Seen in Normotensive obese females and presents with triad of: Ataxia, Urinary incontinence, and Impaired Cognition

CSF circulation and hydrocephalus



IMPORTANT LANDMARKS

- C1 – Hard Palate
- C3 – Hyoid in erect position
- C2 to C3 – Tracheostomy Level Adults , (Dermatome) -> Anterior Neck
- C3 to C4 – Tracheostomy Level Children , (Dermatome) -> Supra and Infraclavicular area
- C3 to C6 – Extent of Larynx
- C4 – BiFOURcation (bifurcation) of Common Carotid Artery
- C6 – Cricoid Level (Esophagus and Trachea Starts) , C6 – Dermatome of Thumb
- T3 to T6 – Oblique Fissure of Lung
- T4 – BiFOURcation (bifurcation) of Trachea, dermatome of Nipple , Prevertebral Fascia extends upto T4
- Extent of Trachea = C6 to T4
- T5 to T6 – Origination of Bronchial Artery
- T6-T7 (dermatome) – Sternal Tip / xiphoid.
- T8 – Caval Opening -> Inferior Vena Cava and Right Phrenic Nerve , Extent of IVC = T8 to L5
- T9 – Xiphisternum
- T10 – Dermatome of Umbilicus , Esophageal Hiatus (Esophagus , Esophageal vessels , and, Vagus nerves)
- T12 – Aortic Opening (Aorta , Azygous , and Thoracic Duct) , Celiac Trunk ,
- Extent of Kidneys = T12 to L3
- Extent of Abdominal Aorta = T12 to L4
- At L1 – Superior Mesenteric Artery , Transpyloric Plane at Lower Level of L1 , End of Adult Spinal Cord , Start of Coccygeal segment of spinal cord.
- L1 to L2 – Cisternae Chyli
- L2 – Renal Artery
- L3 – Inferior Mesenteric Artery , End of Infant Spinal Cord
- L4 – BiFOURcation (bifurcation) of Descending Aorta, Iliac Crest Level (Used in LP)
- L5 – Commencing or Start of L5
- S2– Subarachnoid Space Ends
- Bifurcations – 3 major Bifurcations can be memorized using BiFOURcations
C4 – Common carotid Artery into Internal and External Carotid Arteries, T4 – Tracheal bifurcation
L4 – Descending Aorta into Common Iliac Arteries
Transpyloric Plane is At Lower L1, it passes through following:
Pylorus of Stomach , Fundus of Gallbladder, Hilum of Kidney, First part of Duodenum , Origin of SMA ,
Tip of 9th Costal Cartilage , Lower end of Spinal Cord

IMPORTANT LENGTHS

2.5 cm – Right Bronchus and 5 cm – Left Bronchus
2.5 - 4 cm – Inguinal Canal (1.5 inches)
10 cm – Trachea (13 cm)
12 cm – Spleen
20 cm – Male Urethra (Female Urethra – 4 cm)
25 cm – Duodenum, Esophagus, and Ureters
45 cm – Thoracic Duct, Spinal cord , and Vas Deferens
115 mm – AP diameter of Female Pelvis
5 Micrometer – Diameter of RBC and Blood Capillaries
50 Micrometer – length of Spermatozoa
5 inches – Sigmoid Colon, 10 inches – Ascending Colon and 15 inches – Transverse Colon

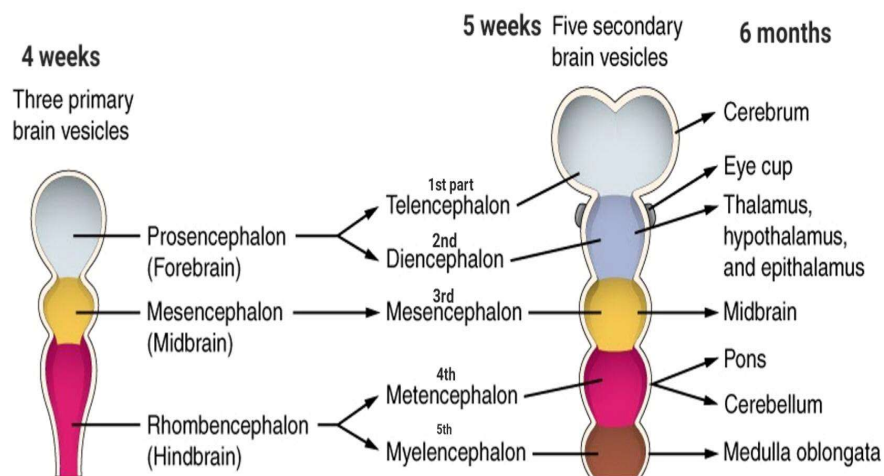
NOTE:

Past Papers BCQs of This Chapter Have Been Discussed in Neuroanatomy Portion.

NEUROANATOMY & CNS PHYSIOLOGY + PATHOLOGY

Classification of Nervous System	
1. Central Nervous system (CNS)	2. Peripheral Nervous system (PNS)
CNS Consists of: a. Brain b. spinal cord	PNS consists of: a. Somatic nervous system (SNS) b. Autonomic nervous system (ANS) ANS is further divided into sympathetic and parasympathetic system.
Neuroepithelia in neural tube gives rise to: i. CNS neurons. ii. CNS glial cells (astrocytes, oligodendrocytes, ependymal cells). Mesoderm gives rise to microglial cells (macrophages).	Neural crest cells give rise to: PNS neurons (dorsal root ganglion, autonomic ganglia) PNS glial cells (Schwann cells, satellite cell) for supporting role. Apart from these Neural crest cells give rise to adrenal medulla, melanocytes, and mesenchyme of facial arches.

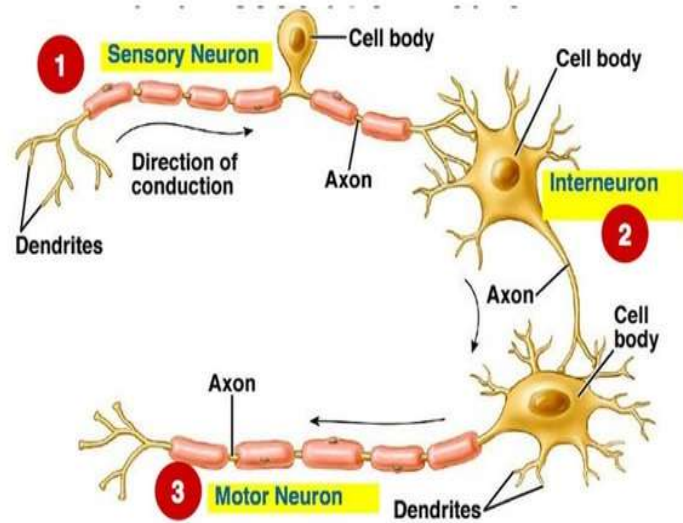
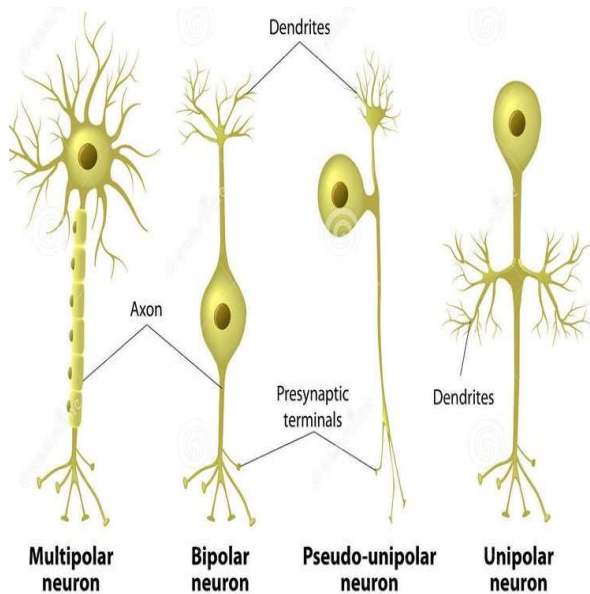
Primary brain vesicles (3 in number)	Secondary brain vesicles (5 in number)	Adult derivative	Cavities
Prosencephalon (Forebrain)	Telencephalon	Cerebral hemisphere Basal ganglia Limbic system	Lateral ventricles
	Diencephalon	Thalamus, subthalamus, epithalamus, retina Hypothalamus, neurohypophysis	Third ventricle
Mesencephalon (Midbrain)	Mesencephalon	Midbrain (Tectum, tegmentum)	Cerebral aqueduct
Rhombencephalon (Hind brain)	Metencephalon	Pons, Cerebellum	Fourth ventricle
	Myelencephalon	Medulla oblongata	



- Notochord induces overlying ectoderm to differentiate into neuroectoderm and form neural plate.
- **Neurulation**: Formation and closure of the neural tube induced by neural plate.
- Neural plate folds give rise to the neural tube, which is open at both ends (anterior and posterior neuropores)
- Anterior neuropores close at day 25 and posterior neuropores close at day 27
- Neural plate gives rise to neural crest cells.
- Notochord becomes the nucleus pulposus of intervertebral disc in adults.

- **Holoprosencephaly** is the failure of embryonic forebrain (Prosencephalon) to separate into 2 cerebral hemispheres during 3rd-4th weeks of development due to mutation of sonic hedgehog pathway. Associated with other midline defects including cleft lip/palate, cyclopia in severe form (fused eyes), Patau syndrome and maternal alcohol use. MRI brain reveals monoventricle + fusion of basal ganglia.
- **Lissencephaly** is the smooth brain lacking sulci & gyri due to failure of neuronal migration associated with microcephaly, ventriculomegaly and hydrocephalus.

NEURON OR NERVE CELL		
<ul style="list-style-type: none"> • Structural and functional unit of nervous system, permanent cells that do not divide. • Has 3 parts → i. Dendrites: carry impulses towards cell body. ii. Cell body/Soma/perikaryon has cytoplasm, nucleus, Nissl's body, neurofibrils, mitochondria and Golgi complex. iii. Axon: carries impulses away from soma. • Neurons are permanent cells i.e. can't divide, due to lack of centrosome. • Speed of nerve regeneration is 1 – 3 mm/day. Marker of neuron are neurofilament protein + synaptophysin. • Cell body and dendrites contain Nissl substance (rough endoplasmic reticulum), absent RER at axon. • Axon Hillock is a region of cell body where axon originates, doesn't contain Nissl granules, have lower threshold than rest of axon due to high sodium channel concentration. • It operates on an "all-or-None" principle (either create an action potential or does Nothing) • Node of Ranvier is a collar of naked axon devoid of myelin sheath, are the sites that permit action potential to jump from node to node → called saltatory conduction. • Nodes of Ranvier are the site of highest voltage gated - Sodium channel concentration. • Saltatory conduction increases the conduction velocity of impulse in Myelinated axon. • Myelination → ↑ membrane resistance and conduction velocity, ↓ membrane capacitance • Myelination in CNS done by Oligodendrocytes and in PNS by Schwann cells. • Most abundant glial cells in CNS white matter are oligodendrocytes, derived from neuroectoderm, have fried egg appearance and each can myelinate approx. 30 axons. They are injured in multiple sclerosis. • Schwann cells are derived from neural crest cells, S – 100 markers, may be injured in Guillain Barre syndrome. • Receptors → sensory neurons → CNS (inter neuron) → Motor neuron → effectors. • Collection of cell bodies is called Ganglia, while Collection of neurons/axons is called nerve. • Endoneurium is a connecting tissue sheath covering individual myelinated nerve fibres, may be affected in GBS. • Perineurium surrounds a fascicle/bundle of nerve fibres. • Epineurium is a dense connective tissue layer that surrounds entire . 		
Structural Classification	Pseudounipolar	Have a single process which divided into two branches close to the cell body e.g., Dorsal root ganglion / sensory ganglia of spinal cord. Sensory neurons are mostly pseudounipolar type.
	Unipolar	have only one process which function as axon e.g., only in mesencephalic nucleus of CN V
	Bipolar	Have 2 process which arise from opposite pole of cell body, one is dendrite while other is axon. Present in retina, olfactory cells (nasal epithelium), cochlea. All of these are special senses neurons or special sensory neurons. Interneurons are of bipolar type also. Olfactory cells are the only neurons in body that replace themselves.
	Multipolar	have a single axon and multiple dendrites e.g., pyramidal cell of cerebral cortex, Purkinji cells in cerebellum and skeletal muscle neurons.
Functional Classification	Sensory	Carry impulses from sensory organs or receptors towards CNS. Have one long dendrite but short axon. They are pseudounipolar mainly.
	Motor	Carry impulses from CNS towards effector organs e.g., skeletal muscles . Mostly they are multipolar type having long axon and multiple dendrites.
	Inter-neurons (Relay neurons)	Associate neurons or relay neurons present in CNS only, not in PNS. Diazepam relaxes skeletal muscles by acting on interneurons. In spinal cord the transmitter released by interneurons at pain inhibiting complex and fibres transmitting is Enkephalin Amacrine cells are inter neurons in retina.



NEUROGLIA CELLS

- They are non-neuronal cells or Supporting cells present in both grey and white matter.
- **In CNS:** astrocyte, microglial cells, oligodendrocytes, and ependymal cells
- **In PNS:** Schwann cells and satellite cells.

Glial cell type	Origin	Location	Functions
Astrocyte	Neuroectoderm Marker - GFAP	CNS	Most common/abundant glial cells in CNS, participate in repair, support, metabolic fuel reserve, component of blood brain barrier, reactive gliosis in response to neural injury.
Microglial cells	Mesoderm	CNS	Phagocytic scavengers, role in defence and immune or inflammatory responses.
Ependymal cells	Neuroectoderm	CNS	Lined by simple columnar ciliated epithelium, form the lining of ventricles and central canal of spinal cord. Specialized ependymal cells in choroid plexus produce CSF. They have cilia to circulate CSF and microvilli for absorption. These cells have No lining membrane/basement membrane
Oligodendrocytes	Neuroectoderm	CNS	Myelination in CNS, fried egg appearance, injured in MS.
Schwann cells	Neural crest cells	PNS	Myelination in PNS, S-100 +ve, injured in GBS.
Satellite cells	Neural crest cells	PNS	Provide structural and metabolic support for neurons.

Chromatolysis

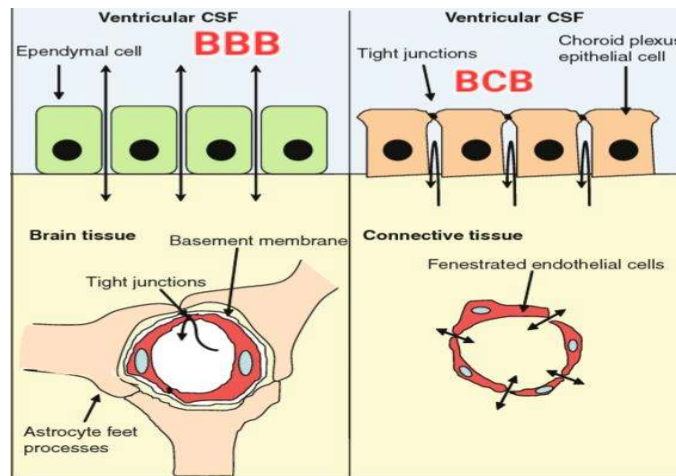
Reaction of neuronal cell body to axonal injury, Changes reflected by **T** protein synthesis in effort to Repair the damaged axon.
Characterized by:

- Round cellular swelling
- Displacement of the nucleus to the periphery
- Dispersion of Nissl substance throughout cytoplasm

Wallerian degeneration

- The disintegration of the axon and myelin sheath distal to site of axonal injury with macrophages removing debris.
- Proximal to the injury, the axon retracts, and the cell body sprouts new protrusions that grow toward other neurons for potential reinnervation.
- Serves as a preparation for axonal regeneration and functional recovery.

Blood Brain Barrier (BBB)	Blood CSF Barrier (BCB)
<p>Formed by 4 structures.</p> <ul style="list-style-type: none"> ➤ Tight junctions between non-fenestrated Capillary endothelial cells ➤ Basement membrane ➤ Astrocyte foot processes ➤ Pericytes <p>BBB = Capillary endothelial cells > Astrocytes (if to choose the single best)</p> <p><u>Significance</u></p> <ul style="list-style-type: none"> ➤ Prevents circulating blood substances. (Bacteria, drugs) from reaching the CSF or CNS ➤ Glucose and amino acids cross slowly by carrier mediated transport mechanisms. Proteins and large amino acids can't cross. ➤ Nonpolar/lipid-soluble substances cross rapidly via diffusion. ➤ Vasogenic edema results from damage to endothelial cells tight junction due to tumor or infarction ➤ Hyperosmolar agents (mannitol) can disrupt BBB. ➤ BBB is absent at: <ul style="list-style-type: none"> a. area postrema (vomiting after chemotherapy) b. Organum vasculosum lamina terminalis (OVLt): osmoreceptors/neurosecretory products to enter circulation e.g., ADH. 	<p>It is formed by</p> <ul style="list-style-type: none"> ➤ Tight junction's b/w Capillary endothelial cells in the choroid plexus ➤ Basement membrane ➤ Specialized ependymal cells ➤ It is not present in whole brain like BBB but it is only limited to lateral, 3rd and 4th ventricles (the places where CSF produces+ flows) ➤ BCB is less permeable (less leaky) than BBB ➤ 75cm² surface area of BCB as compared to 155cm² of BBB. ➤ BCB = ependymal cells > capillary endothelial cells



- Grey matter is composed of nerve cell bodies embedded in neuroglia whereas white matter is made of nerve cell bodies embedded in neuroglia. White color due to myelin sheath
- In spinal cord grey matter is inside and white matter is outside.
- In cerebrum + cerebellum: white matter is inside, and grey matter is outside.
- Most common glial cells are astrocytes and most common cells or abundant in white matter are oligodendrocytes.
- Most abundant astrocytes in white matter are Fibrous astrocytes.
- Most abundant astrocytes in grey matter are protoplasmic astrocytes.
- Cells causing hindrance in CNS repair/regeneration following injury are oligodendrocytes.
- Regeneration of brain cells cannot occur due to → Oligodendrocytes. (Because these cells start myelination and way faster than the regeneration/repair by astrocytes, therefore create trouble for repair process).
- Mesaxons are pair of parallel plasma membrane, a feature of Schwann cells.
- Axonal Myelination/peripheral nerve in fetus begins at 04 months and continues after birth (2 – 3 years)
- Myelination of cranial nerves begins at 06th month.

SENSORY SYSTEM			
Types of Sensory Receptors			
Mechanoreceptors	Chemoreceptors	Photoreceptors	Extreme of Temp + pain
<ul style="list-style-type: none"> Baroreceptors Hair cells in ear Stretch receptors in muscles (muscle spindle) Pacinian corpuscles Joint receptors 	<ul style="list-style-type: none"> Olfactory receptors Taste receptors Carotid body O₂ receptors Osmoreceptors 	Also known as electromagnetic receptors E.g Rods and Cons	<ul style="list-style-type: none"> Nociceptors -- meninges contain nociceptors. Thermo-receptors have long receptive field

SENSORY RECEPTORS			
Type	Fibre type	Location	Senses
Pacinian corpuscles	Large myelinated and encapsulated. Fastest adaptation Phasic receptors	Dermis - not in epidermis, periarticular (joints, ligaments) Onion skin shaped	High frequency vibration (40-400 HZ) Detect tuning fork frequency. Deep touch Main sensation encoded = vibration/tapping
Meissner's corpuscles	Large myelinated and encapsulated. Adapt quickly	Abundant on fingertip Glabrous (Hairless) skin	Dynamic fine/Light touch, tactile 2-point discrimination, skin indentation Low frequency vibration upto 40 HZ. Sensation encoded = velocity
Merkel disc	Large myelinated Uncapsulated Adapt slowly	Superficial skin Fingertips	Iggo dome receptors are the Markel discs. Detect deep static or steady touch (shapes/edges) Sensation encoded = location, also detect pressure.
Ruffini Corpuscles	Large myelinated Slowly adapt	Fingertips Joints	Deep static or steady pressure, stretch, joint angle changes, warmth, Large receptive field
Krause end bulbs	Slow adaptation	Skin, lips, mucous membrane, genitals.	Detect cold
Free nerve endings	A delta: myelinated, for fast pain C: unmyelinated, slow,	All tissues, numerous on skin. Not present on lens and cartilage.	Pain Temperature

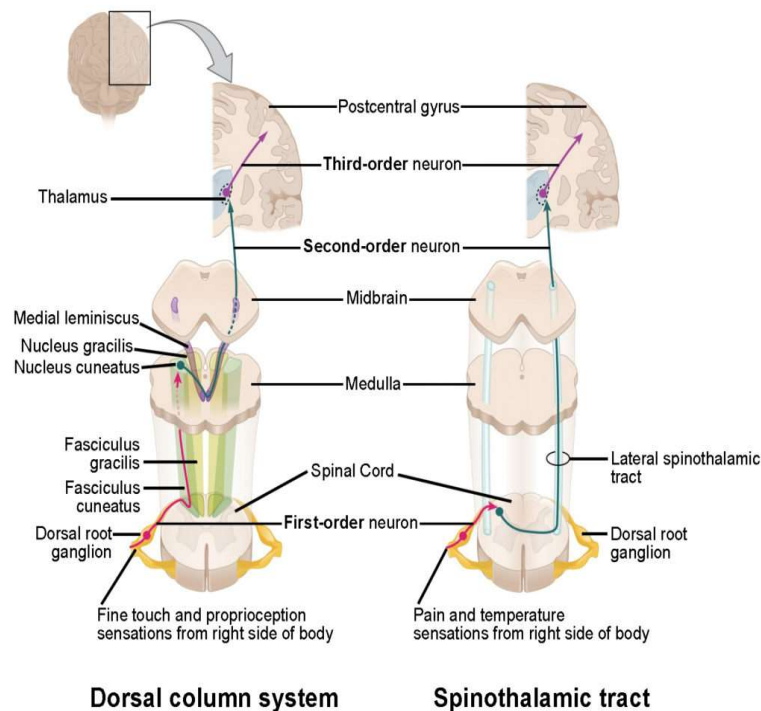
- Deep touch → Pacinian corpuscles, deep static/steady touch → Merkel disc
- Deep static/steady pressure, warmth → Ruffini corpuscles, For Cold → Krause end bulbs
- Never adapt = baroreceptors > temperature receptors
- **Receptive field** is an area of the body that, when stimulated, changes the firing rate of a sensory neuron.
- If the firing rate of the sensory neuron is increased, the receptive field is excitatory.
- If the firing rate of the sensory neuron is decreased, the receptive field is inhibitory.
- Large receptive field → Ruffini corpuscles and long receptive field → temperature/Thermoreceptors
- **Slowly adapting** or tonic receptors (muscle spindle; pressure; slow pain) Respond repetitively to a prolonged stimulus and detect a steady stimulus.
- **Rapidly adapting** or phasic receptors (Pacinian corpuscle; light touch) Show a decline in action potential frequency with time in response to a constant Stimulus. Primarily detect onset and offset of a stimulus.
- The change in membrane potential produced by the Stimulus is the receptor potential or generator potential.
- Stimulus arrives at the sensory receptor. The stimulus may be a photon of light on the retina, a molecule of NaCl on the tongue. Ion channels are opened in the sensory receptor, allowing current to flow. Usually, the current is inward, which produces depolarization of the receptor.
- The exception is in the photoreceptor, where light causes decreased inward current and hyperpolarization.
- Receptor potentials are graded in size depending upon size of stimulus.

ERLANGER AND GASSER CLASSIFICATION OF NERVE FIBERS			
General Fiber type (Sensory and Motor) (A – C)	Sensory Fibers type (Class I – IV)	Diameter	Conduction velocity
A Type (Alpha to delta, all Heavily myelinated) A – alpha (proprioception and somatic motor) Example: Large alpha motor neurons	I (myelinated) Ia: muscle spindle afferents Ib: Golgi tendon organs	Largest Largest	Fastest Fastest
A – beta Example: Touch, pressure	II: (myelinated) touch, pressure, secondary afferents of muscle spindles	Medium	Moderate
A – gamma Example: gamma motor neurons to muscle spindle (intrafusal fibres)	–	Medium	Moderate
A – delta Example: Fast pain, temperature (cold), touch, pressure, nociception	III: (myelinated) Fast pain, temperature, touch, pressure	Small	Moderate
B (myelinated) Example: pre-ganglionic autonomic fibres (Purely autonomic fibres)	–	Small	Moderate
C (Unmyelinated) post-ganglionic autonomic fibres, slow pain, itch, warmth sensation, olfaction	IV: (Unmyelinated) pain, temperature, olfaction	Smallest	Slowest

MAIN CONCEPT (Very Important)

- Type A – C are general fibres (sensory and motor function)
- numerical types I – IV are only sensory fibres.
- While going down from A → C and I → IV, conduction velocity, diameter, and myelination decreases
- Diameter and conduction velocity sequence: A alpha > A beta > A gamma > A delta > B > C.
- An alpha and Ia, Ib being the fastest fibres, having largest diameter and heavily myelinated.
- Type C & IV are unmyelinated, smallest, and slowest.
- Spike duration and absolute refractory period are opposite to diameter. C > B > A delta > A gamma > A beta > A alpha
- A Fibers have further four types --- alpha, beta, gamma, and delta
- Alpha & A gamma fibres are motor (fibres to muscle spindles)
- A alpha supply → extrafusal fibers, while A gamma supply the → intrafusal fibers.
- An alpha and Ia → afferents (sensory) to **muscle spindles**, A- alpha also deals with **proprioception**.
- An alpha and Ib → **Golgi tendon** organs
- A beta and II → **touch, pressure**, muscle spindles, flower spray endings (slow, static response to length changes)
- A delta and III → pain, cold. For **Fast pain - A delta** fibres.
- Spinothalamic tract contains A delta, C fibres, Class III + IV fibers.
- Type B → purely autonomic, pre-ganglionic autonomic fibres
- Type C and IV → pain and temperature. For slow pain (aching, burning, throbbing) – type C fibers (dorsal root)
- Type C has two roots dorsal (for **slow pain**, temperature) and an autonomic (post-ganglionic autonomic fibers)
- Neurotransmitter for fast pain is glutamate, but for slow pain → substance P.
- Inhibition of substance P is the basis for pain relief by Opioids.
- Nociception via A delta and C type fibers.
- Type A are most effected by Pressure while Hypoxia effects mostly Type B, and, Anaesthesia effects → type C
- Only receptor having both sensory and motor innervation → Muscle spindle (A alpha and A gamma)
- Dorsal column medial lemniscus system (DCML) contains A beta + Class II fibers → touch, pressure.
- Stretch reflex /Myotatic reflex (via muscles spindles) → type 1a fibers involved.
- Inverse stretch reflex (via Golgi tendon) → type Ib fibers involved.
- Withdrawal reflex/Flexor reflex via Free nerve endings → type II, III, IV fibers involved.

Organization of Sensory system (Sensory Pathway from Sensory receptor to Cerebral cortex)			
<ul style="list-style-type: none"> Sensory receptors are activated by environmental stimuli. Sensory receptors may be specialized epithelial cells (e.g photoreceptors, taste receptors) or primary afferent neurons (e.g., olfactory chemoreceptors), Transduce the stimulus into electrical energy (i.e., receptor potential). 			
First order neurons	Second order neurons	Third order neurons	Fourth order neurons
<ul style="list-style-type: none"> The primary afferent neurons that receive the transduced signal and send the Information to the CNS. Cell bodies of the primary afferent neurons are in dorsal Root or spinal cord ganglia. 	<ul style="list-style-type: none"> located in the spinal cord or brain stem Receive information from one or more primary afferent neurons in relay nuclei and transmit it to the thalamus. Axons of second-order neurons may cross the midline in a relay nucleus in the spinal cord before they ascend to the thalamus. Therefore, sensory information originating on one side of the body ascends to the contralateral thalamus. 	<ul style="list-style-type: none"> Located in the relay nuclei of the thalamus. From there, encoded sensory information ascends to the cerebral cortex 	<ul style="list-style-type: none"> Located in the appropriate sensory area of the cerebral cortex. The information Received results in a conscious perception of the stimulus



- Fibers of dorsal column decussate/cross midline in the brain stem (medulla)
- Fibers of anterior Spinothalamic tract decussate/cross midline in the spinal cord
- 1st order neuron arises in DRG/spinal cord
- 2nd order arises from spinal cord or brain stem → Thalamus (so axons of 2nd order are in thalamus).
- 3rd order neurons extend from thalamus to Cerebral cortex (post central gyrus – sensory cortex)
- Cerebral cortex has sensory areas SI & SII. S1 has same somatotopic representation same as thalamus.
- This map of body is known as Sensory Homunculus. The largest areas represent the face, hands, and fingers.
- Principal sensory area of cortex (Brodmann area 3, 1, 2). Somesthetic association area (Brodmann area 5 & 7)
- Referred** pain is the pain of visceral origin that is referred to sites on skin following the dermatome rule. These sites are innervated by the nerves arising in the same segment of spinal cord e.g Pain of IHD or MI is referred inner left arm due to Intercostobrachial nerve (T2) supplying that particular site.

MOTOR SYSTEM

Motor unit

- Consists of a single motor neuron and the muscle fibers that it innervates.
- For fine control (e.g Muscles of the eye), a single motoneuron innervates only a few muscle fibers.
- For larger Movements (e.g postural muscles), a single motor neuron may innervate thousands of Muscle fibers.
- The motor neuron pool is the group of motoneuron that innervates fibers within the same Muscle.
- **Small motoneurons** Innervate a few muscle fibers, fire first due to the lowest thresholds and therefore, generate the smallest force.
- **Large motoneurons** have the highest thresholds and, therefore, fire last. Innervate many muscle fibers and generate the largest force.

Muscle sensor

1. Muscle spindles (groups Ia and II afferents) are arranged in parallel with Extrafusal Fibers. They detect both static and dynamic changes in muscle length (stretch)
2. Golgi tendon organs (group Ib afferents) are arranged in series with extrafusal fibers. They detect muscle tension. (T- Tension and tendon)
3. Pacinian corpuscles (group II afferents) are distributed throughout muscle.
4. Free nerve endings (groups III and IV afferents) detect noxious stimuli,

Types of muscle fibers➤ **Extrafusal fibers:**

- Make up the bulk of muscle, innervated by alpha motoneuron.
- Provide the force for muscle contraction.

➤ **Intrafusal fibers:**

- smaller than extrafusal fibers, innervated by gamma (γ) motoneuron, encapsulated in sheaths to form muscle spindles.
- Run in parallel with extrafusal fibers, but not for the entire length of the muscle and are too small to generate significant force.

Muscle spindles & Stretch Reflex

- They are distributed throughout muscle and consist of small, encapsulated intrafusal fibers connected in parallel with large force generating extrafusal fibers.
- The finer the movement required, the greater the number of muscle spindles in a muscle.

Types of intrafusal fibers

1. **Nuclear bag fibers:** Detect the **rate of change in muscle length** (fast, dynamic changes). They are innervated by group Ia afferents and have nuclei collected in a central “bag” region.
2. **Nuclear chain fibers:** Detect **static changes in muscle length** and innervated by group II afferents. They are more numerous than nuclear bag fibers and have nuclei arranged in rows.

Mechanism of Muscle Spindles:

- Muscle spindle reflexes oppose (correct for) increases in muscle length (stretch)
- Sensory information about muscle length is received by group Ia (velocity) a Group II (static) afferent fibers.
- When a muscle is lengthened/stretched → muscle spindle is also stretched → stimulation of grp Ia + II fibres.
- Group Ia afferents stimulate alpha motoneurons in spinal cord → contraction + shortening of muscle.
- Thus, the original stretch is opposed, and muscle length is maintained.
- At the same time synergistic muscles are activated and antagonistic muscles are inhibited.
- ✓ Alpha + gamma motoneuron are co-activated so that muscle spindles remain sensitive to changes in muscle length during contraction.
- ✓ Gamma motoneuron activity increases the sensitivity of muscle spindle.

Example of Myotatic or Stretch Reflex (Knee reflex)

Monosynaptic reflex, group Ia afferents, muscle is stretched → leads to contraction of muscle, as explained below:

- ✓ Tapping on patellar tendon causes Quadriceps to stretch. Stretch of quadriceps stimulated group Ia afferent fibers which activate alpha motoneurons that make the quadriceps contract. Contraction of quadriceps forces the lower leg to extend.
- ✓ Gamma motoneuron activity increases the sensitivity of muscle spindle and therefore exaggerate the knee jerk reflex.

Golgi Tendon Organ & Inverse Stretch reflex/Inverse Myotatic reflex

- Di synaptic reflex - the opposite or inverse of the stretch reflex.
- Active muscle contraction stimulates the Golgi tendon organs and group Ib afferent fibers.
- The group Ib afferents stimulate inhibitory interneurons in the spinal cord. These inter-Neurons inhibit a-motoneurons and cause relaxation of the muscle that was originally contracted and prevents muscle tear.
- At the same time, antagonistic muscles are excited.

Example:

- Clasp-knife reflex, an exaggerated form of the Golgi tendon reflex, can occur with disease of the corticospinal tracts (hypertonicity or spasticity)
- For example, if the arm is hypertonic (while lifting heavy books/weight) the increased sensitivity of the muscle spindle in the extensor muscles (triceps) causes resistance to flexion of the arm.
- Eventually Tension in the triceps increases to the point at which it activates the Golgi tendon Reflex, causing the triceps to relax and the arm to flex closed like a jack knife.

Flexor withdrawal reflex

- **Polysynaptic reflex** (other polysynaptic reflexes in body are superficial Abdominal + cremasteric reflex)
- Results in flexion on the ipsilateral side and extension on the contralateral side
- Somatosensory and pain afferent fibers elicit withdrawal of the stimulated body part from the noxious stimulus.

Example:

While touching a Hot object Pain (touching a hot stove) stimulates the flexor reflex afferents of groups II, III and IV.

- The afferent fibers synapse polysynaptically (via interneurons) onto motoneurons in the spinal cord
- On the ipsilateral side of the pain stimulus, flexors are stimulated (they contract) and Extensors are inhibited (they relax), and the arm is jerked away from the stove.
- On the Contralateral side, flexors are inhibited, and, extensors are stimulated (crossed extension reflex) to maintain the balance.
- As a result of persistent neural activity in the polysynaptic circuits, an after discharge occurs.
- The after discharge prevents the muscle from relaxing for some time.

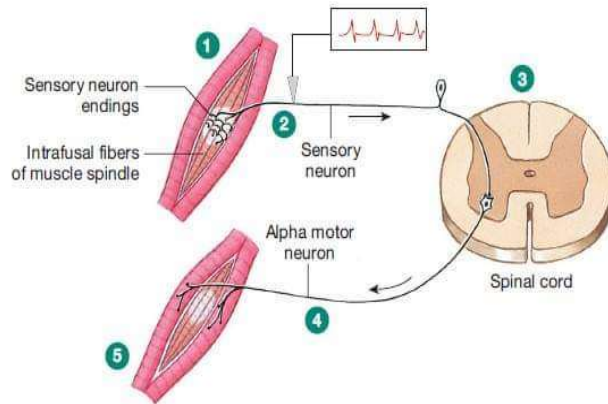
SUMMARY

- Muscle fibres innervated by a single motor neuron = Motor unit.
- Muscles fibres are:
Intrafusal fibres (innervated via Alpha motoneuron) and extrafusal fibres (innervation via gamma- γ motoneurons)
- Intrafusal fibres of muscle spindles have nuclear bag fibres (detect dynamic changes in muscle length) and nuclear chain fibers (detect static changes in muscle length)
- Muscles spindles respond to changes in muscles length or stretch to muscle, afferents via Ia fibers.
- Golgi organs respond to changes in muscle tension, so prevent muscle tear, afferents via Ib fibers.
- Nociception (extreme pain/temperature) stimulates flexor reflex (Withdrawal reflex)
- Regarding Stretch reflex (e.g Knee Jerk) → monosynaptic, muscle spindles and Ia fibers involved, stretching the muscle causes contraction of muscle (original length maintained). Stimulus = Stretch, Response = Contraction.
- Golgi tendon reflex or inverse stretch reflex (e.g clasp-knife) → disynaptic, Golgi tendon +Ib fibers involved
Stimulus = Muscle contraction and Response = Relaxation of muscle.
- Flexor withdrawal reflex → Polysynaptic, nociceptors and group II, III and IV fibers involved.
Stimulus = Pain and Response = ipsilateral flexion + contralateral extension.

SPINAL ORGANIZATION OF MOTOR SYSTEM

Convergence	Divergence	Recurrent inhibition
<ul style="list-style-type: none"> ➤ It occurs when a single alpha motoneuron receives its input from many muscle spindles group Ia afferents in the homonymous muscle. ➤ Homonymous muscles mean the same muscle that was stretched. 	<ul style="list-style-type: none"> ➤ Occurs when muscle spindle group Ia afferent fibers project to all alpha motoneurons that innervate the homonymous muscle 	<ul style="list-style-type: none"> ➤ Renshaw cells are inhibitory neurons in ventral horn of the spinal cord. ➤ Receive input from collateral axons of motoneurons.

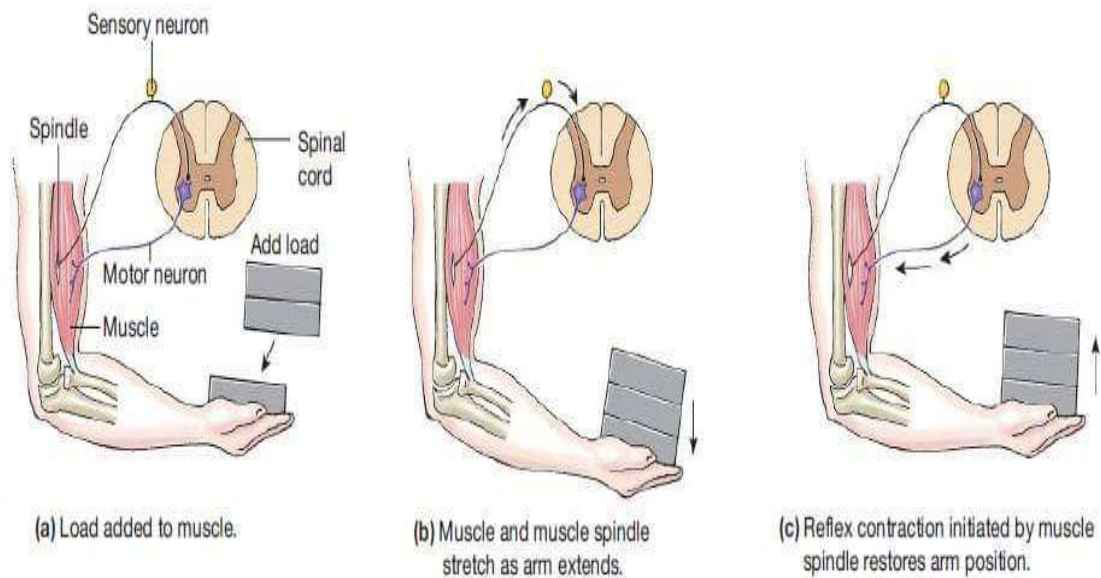
- Convergence produces spatial summation when multiple inputs bring threshold instead of single.
 - Convergence produces temporal summation when inputs arrive in rapid succession.
- Upon stimulation, they inhibit the motoneuron via feedback inhibition.



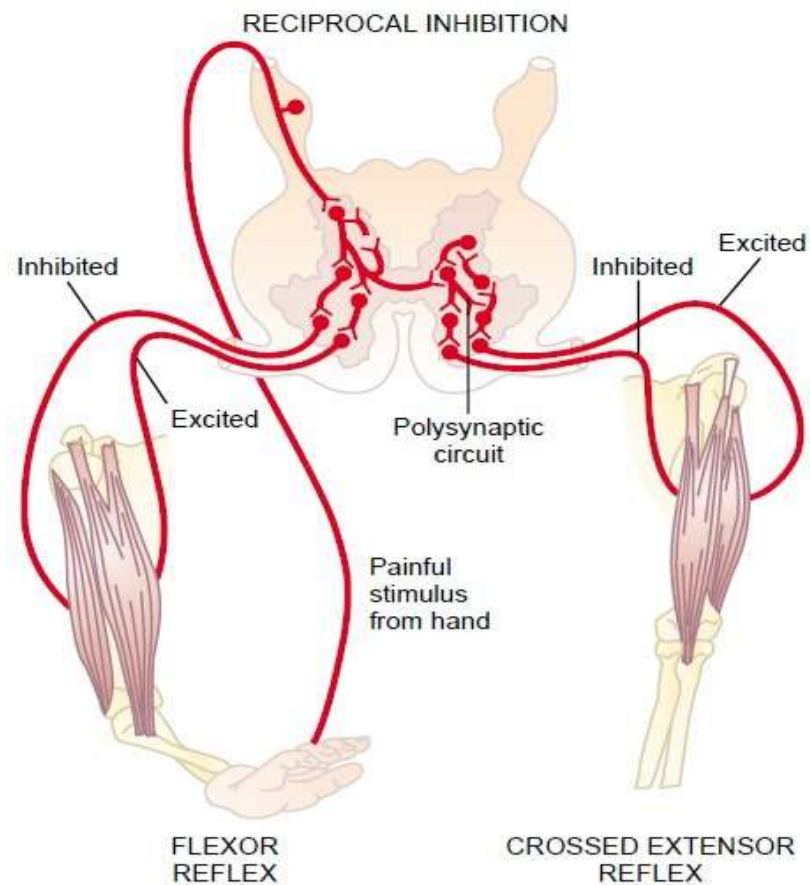
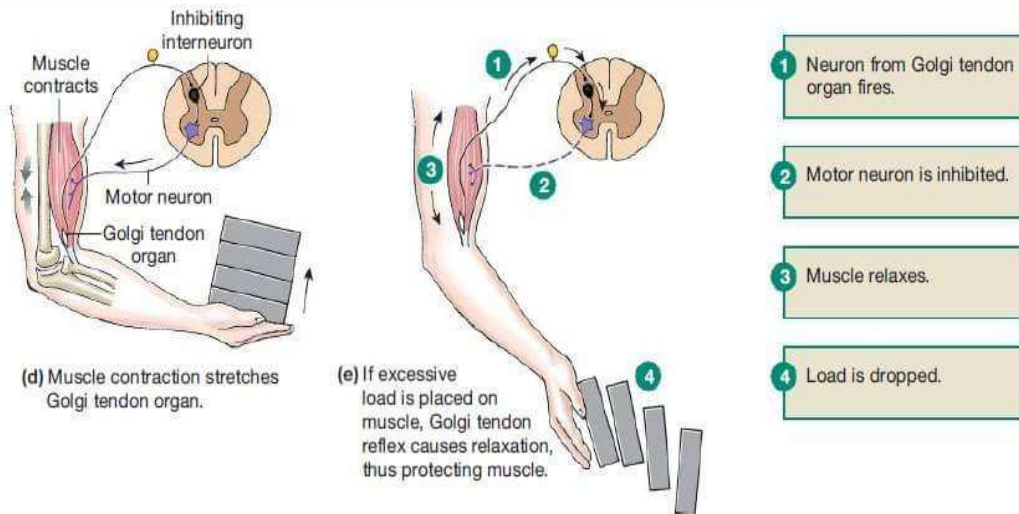
(a) Spindles are firing even when muscle is relaxed.

- 1 Extrafusal muscle fibers at resting length
- 2 Sensory neuron is tonically active.
- 3 Spinal cord integrates function.
- 4 Alpha motor neurons to extrafusal fibers receive tonic input from muscle spindles.
- 5 Extrafusal fibers maintain a certain level of tension even at rest.

Muscle spindle reflex: the addition of a load stretches the muscle and the spindles, creating a reflex contraction.



Golgi tendon reflex protects the muscle from excessively heavy loads by causing the muscle to relax and drop the load.



AUTONOMIC NERVOUS SYSTEM (ANS)

- ANS is different from Somatic nervous system which innervates skeletal muscles.
- ANS innervates and regulates Smooth muscles, cardiac muscles, and glands.
- Sympathetic, parasympathetic nervous systems and enteric nervous system belongs to the ANS.
- Sympathetic and parasympathetic system are composed of pre-ganglionic and post-ganglionic neurons.
- **Ganglion:** A cluster of interconnecting nerve cells bodies outside the brain.
- Autonomic ganglia are clusters of neuron cell bodies that transmit sensory signals from the Periphery to the integration centres in the CNS.
- In the autonomic nervous system, fibers from the CNS to the ganglion are known as preganglionic Fibers.
- All preganglionic fibers of the ANS are cholinergic – means that they have acetylcholine as their Neurotransmitter and are myelinated for faster transmission.
- Postganglionic Fiber: These are the fibers that run from the ganglion to the effector organ.
- In both division of the autonomic nervous system, postganglionic neurons express nicotinic Acetylcholine receptors to receive signals from Preganglionic neurons.
- Both nervous systems control physiological processes of the body (respiration, digestion, Circulation, urination, and reproduction). They participate in maintaining homeostasis of the Body.

Characteristics	Sympathetic	Parasympathetic	Somatic
Origin of pre-ganglionic nerve	Thoraco-lumbar outflow T1 – L3 of segment of spinal cord	Cranio-sacral outflow Nuclei of CN 3, 7, 9, 10 Sacral segments S2-S4	
Location of autonomic ganglia	Paravertebral chain	Near effector organs	
Length of pre-ganglionic nerve	Short	Long (because they arise from CNS – travel long)	
Length of post-ganglionic nerve Axon	Long	Short	
Neurotransmitter released by pre-ganglion & post-ganglionic nerve fibers	Pre-ganglionic fibers: ACh Post-ganglionic cholinergic fibers: ACh (sweat glands) Post-ganglionic adrenergic fibers: Nor-epinephrine.	Pre-ganglionic fibers: ACh Post-ganglionic fibers: ACh	
Receptor type in Ganglion	Nicotinic	Nicotinic	
Neurotransmitter in ganglion	ACh	ACh	
Neurotransmitter in effector organs	Nor-epinephrine, except sweat glands (ACh)	ACh	ACh (in synapse)
Effector organs	Smooth muscles, cardiac muscles, and glands.	Smooth muscles, cardiac muscles, and glands.	Skeletal muscles
Receptor types in effector organs	Alpha 1, 2 , Beta 1, 2	Muscarinic	Nicotinic

Important Concepts

- **Adrenergic neurons** release NE as neurotransmitter whereas cholinergic neurons release ACh as neurotransmitter.
- ACh is used by → pre-ganglionic parasympathetic + post-ganglionic parasympathetic + pre-ganglionic sympathetic.
- NE is used by → only post-ganglionic adrenergic fibers of sympathetic system.
- Whereas cholinergic post ganglionic sympathetic fibers to sweat glands use → ACh as neurotransmitter.
- Regarding Adrenal medulla: pre-ganglionic fibers of sympathetic system synapse directly on Chromaffin cells.
- Chromaffin cells secrete 80% epinephrine and 20% nor-epinephrine into circulation.
- Non adrenergic, noncholinergic neurons include some post-ganglionic parasympathetic neurons of GIT, which release Nitric oxide, substance P and vasoactive intestinal peptide (VIP)
- SANS → fight / flight response – main effect on CVS.
- PANS → rest / digest – main effect on GIT & glands.

RECEPTORS IN ANS

- A. **Cholinergic receptors** (Cholinoreceptors): They are of Muscarinic and Nicotinic type.
 Muscarinic: M1, M2, M3, M4 and M5.
 Nicotinic: NN (autonomic ganglia) and NM (Neuromuscular junction) → use Ach → Opening of ion channels.
- B. **Adrenergic receptors** (adrenoreceptors): Alpha 1, alpha 2, beta 1, beta 2 and beta 3.
- **Note:** M1 – M3, Alpha 1,2 and beta 1,2,3 are G-protein linked, using 2nd messengers
 - **G Protein Types:** Gq, Gs (stimulatory) and Gi type (inhibitory)
 - **Gq** uses Phospholipase C & IP3 as 2nd messenger whereas Gs and Gi use cAMP
 - M1, M3, M5 and alpha 1 receptor use Gq protein → Phospholipase C & IP3 → Ca⁺ ↑
 - **Gi** protein is used by **Alpha 2** and **M2**, so they are inhibitory in nature, involve Dec. cAMP → ↓ Ca⁺ and ↑ K⁺
 - Beta1 uses **Gs** → ↑ cAMP formation leads to elevated Ca²⁺ levels.
 - Beta 2 and beta 3 use both Gs and Gi depending upon location
 - B1 & M2 on Heart, B1 on kidney (JG cells), B2 on lungs, alpha 1 on sphincters, alpha 2 present in CNS.
 - **B2** is present on vasculature of skeletal muscles causing vasodilation and inc. Blood flow during exercise.
 - **M3**, B2 and B3 present on detrusor muscle of bladder. Alpha 1 and beta 1 on uterus.
 - Alpha 1 receptors abundant on proximal urethra and neck of bladder, also present in GIT vessels, sphincters and platelets. Lipolysis is mediated via Beta1 > B3.

Organ	Sympathetic receptor and effect (Fight & Flight response)	Parasympathetic receptor and effect (Rest & Digest)
CNS	Alpha 1,2, B1, B2 Alpha 2 is inhibitory – decrease sympathetic outflow from CNS and decrease the B. P	M1 , M5. M1 are involved in cognitive and memory process using ACh
Eye	Alpha 1 → pupillary dilator muscles contraction causes Mydriasis (far vision) B2 – increases aqueous humour production	M1 → constricts the sphincters pupillae → Miosis. For Near vision M3 constricts ciliary muscles – accommodation.
Heart	B1 → ↑ HR, contractility, and AV nodal conduction Or decrease the delay of AV node. Sympathetic system mainly affects CVS.	M2 → ↓ HR, contractility, and AV nodal conduction Or increased AV nodal delay.
Lungs	B2 → dilatation of bronchial smooth muscles causing bronchodilation	M3 → constriction of bronchial smooth muscles or bronchoconstriction
GIT	Alpha1,2 and beta 2 Alpha 1 – constricts sphincters. Sympathetic stimulation decreases GI motility and peristalsis	M3 – inc. GIT motility/peristalsis + Relaxation of sphincters. M1 stimulates enteric nervous system Parasympathetic system mainly effects GIT and glands
Liver	B2 – increase glycogenolysis in liver	--
Male.sex organs	Alpha receptors mediate Emission > Ejaculation. Ejaculation is mainly via Pudendal nerves (S2, S3, S4)	Parasympathetic stimulation causes Erection.
Kidney	B1 – increase Renin secretion	--
Vessels	Alpha 1- constrict blood vessel in vascular smooth muscles (skin, splanchnic circulation) Beta 2 – vasodilation of skeletal muscles vessels.	-- M3 causes endothelium mediated vasodilation
Bladder neck + prostate	Alpha 1 abundant – constriction of bladder sphincter B3 also in excess – mediate bladder relaxation	M3 – bladder constriction for micturition and sphincter relaxation.
Fat cells	B1 > B3 mediate Lipolysis Alpha 2 inhibits the lipolysis.	--
Sweat glands	Sympathetic cholinergic increases sweating.	No effect/ inc secretion in some experimentations.
Lacrimal + Salivary glands	Decreased secretion of glands (lacrimal, salivary, and gastric glands) Copious, thick saliva by alpha 1 & beta 1 receptors	M3 → Inc secretion of all glands, gastric juice, except sweat glands.
Metabolic effects	B2 cause ↑ insulin release Alpha 2 dec the insulin release	M3 inc the insulin release

	B3 inc thermogenesis in skeletal muscles	
Platelets	Alpha 2 inc. aggregation of PLT	--
Uterus	B2- decreases the tone of uterus, used for tocolysis in pre term labour.	--

Important Facts

- c. Main systems effected by Parasympathetic systems are GIT & Gland whereas Heart & Blood vessels are mainly affected by Sympathetic system.
- d. Parasympathetic is the system of nature i.e required for normal optimum functioning.
- e. Autonomic centres in brain stem and hypothalamus are as follows.

Medulla	Pons	Midbrain	Hypothalamus
Vasomotor center Respiratory centre Swallowing, cough, and vomiting centres	Pneumotaxic center Main Micturition center (Facilitatory)	Micturition – inhibitory center	Temperature regulation Thirst and food intake i.e Vegetative functions. Main center for autonomic control is Hypothalamus.

CEREBRAL CORTEX (CEREBRUM)

Features	Layers & Lobes	Dominance				
<ul style="list-style-type: none">• Largest part of brain, made of two hemispheres joined by corpus callosum and separation b/w them is by median longitudinal fissure.• surface of brain is folded into sulci (depressions) and gyri (raised areas)• Four main sulci are:<ol style="list-style-type: none">1. Lateral sulcus of Sylvius (secondary): has a stem + 3 rami.<ul style="list-style-type: none">▪ insula is called the central lobe, a hidden portion of cerebral cortex in floor of lateral sulcus.MCA supplies insula and runs in lateral sulcus.2. Central sulcus of Ronaldo (The limiting sulcus):<ul style="list-style-type: none">• gyrus that lie anterior to it is the pre-central gyrus (controls motor movements of opposite side.• gyrus that lie posterior to it is the post-central gyrus (controls sensory functions of opposite side).• Central sulcus divides insula into anterior and posterior parts• Anterior region has three short gyri called gyri brevia and posterior region has 1 or 2 long gyri called gyri longa.3. Calcarine sulcus (complete sulcus): on medial surface of cerebral hemisphere4. Parieto-occipital sulcus: (secondary sulcus) begins at midpoint of Calcarine sulcus.	<p>Neocortex: six layered Alloccortex: three layered. Six layers are as follows.</p> <ol style="list-style-type: none">1. Molecular layer2. External granular layer3. External pyramidal layer4. Internal granular layer – receives thalamo-cortical inputs.5. Ganglionic layer – internal pyramidal layer that gives rise to corticospinal and corticobulbar tracts.6. Multiform layer: layer of polymorphic cells<ul style="list-style-type: none">○ In sensory cortex layer IV is thickest○ In motor cortex layer V is thickest○ The motor cortex is also known as the agranular cortex because of the masking (attenuation) of the granular layers, particularly the inner granular layer.○ The somatosensory cortex is different from primary motor cortex in granular layer○ The areas of cortex in which 6 layers are recognized are called homotypical.○ ▪ Heterotypical refers to those areas lacking basic 6 layers.○ 4 lobes of brain: Frontal, parietal, temporal, and, occipital.	<p>More than 85% of adult population is right-handed → left hemisphere is dominant. About 90% of adult population is left hemisphere dominant for speech. Non-dominant hemisphere is right hemisphere in right-handed people.</p> <table><tr><th>Dominant hemisphere or Categorical</th><th>Non-dominant or Representational</th></tr><tr><td>Controls:<ul style="list-style-type: none">• Handedness• Language, Speech• Analytical reasoning• Functional areas of behaviour.</td><td>Controls:<ul style="list-style-type: none">• spatial perception (body language)• Recognition of faces and music themes• Recognition of objects by their forms.</td></tr></table> <p>Left hemisphere (dominant in right-handed) is for = verbal + analytical role E.g logical reasoning, reading, writing, mathematics, receives sensation from right side of body and control movements on right side of the body.</p> <p>Right hemisphere (non-dominant in right-handed): is for = Non-verbal functions e.g creativity, recognition of patterns, faces, music, appreciation of art, emotional detection and expression, control movements on left side of body and spatial ability.</p>	Dominant hemisphere or Categorical	Non-dominant or Representational	Controls: <ul style="list-style-type: none">• Handedness• Language, Speech• Analytical reasoning• Functional areas of behaviour.	Controls: <ul style="list-style-type: none">• spatial perception (body language)• Recognition of faces and music themes• Recognition of objects by their forms.
Dominant hemisphere or Categorical	Non-dominant or Representational					
Controls: <ul style="list-style-type: none">• Handedness• Language, Speech• Analytical reasoning• Functional areas of behaviour.	Controls: <ul style="list-style-type: none">• spatial perception (body language)• Recognition of faces and music themes• Recognition of objects by their forms.					

SPECIAL AREAS OF BRAIN (BRODMANN AREAS)			
Brodman No.	Area name	Brodman No	Area name
3, 1, 2 Posterior central gyrus - parietal lobe	Primary or principal sensory area (Or) primary Somaesthetic area	22 (superior temporal gyrus of dominant lobe)	Secondary auditory area Sensory speech area/Wernicke's area
4 Lies in Precentral gyrus (frontal lobe)	Primary motor area (Primary motor cortex) ■ Lesion results in pure motor signs	28 (Located in uncus)	Entorhinal cortex (olfactory area)
5, 7 (lies in superior parietal lobule) parietal lobes	Somesthetic association area ■ lesion results in astereognosis	39 (In posterior parietal lobe)	Angular gyrus ■ lesion results in agraphia + alexia. acalculia, anomia
6 (in anterior part of pre-central gyrus, posterior of superior middle, inferior frontal gyri	Premotor area ■ image of the movement to be performed forms in this.	41,42 (Heschl's gyrus in superior portion of superior temporal gyrus)	Primary auditory area (Sup temporal gyrus in inferior wall of lateral sulcus)
8,9 (Frontal lobe)	Frontal eye field ■ Lesion results in conjugate deviation of eye towards lesion side.	43	Taste area (at lower end of post central gyrus in superior wall of lateral sulcus)
9,10,11,12 (Ant frontal lobe)	Pre-frontal cortex: anterior part of frontal lobe	44, 45-	Motor speech area (Broca's area) (At Posterior Part of Inferior frontal gyrus)
17 -calcarine sulcus	Primary visual cortex	For face recognition → inferior temporal lobe (area 20, 21) and both occipital lobes (parieto-temporo occipital lobe) Lesion results in prosopagnosia (unable to recognize faces) Fusiform gyrus involved.	
18,19 (Occipital lobe)	Secondary visual area or visual association area		

Brain Lobe	Functions and important Areas		Disorders/Lesions result in	
Frontal lobe	<ul style="list-style-type: none"> Largest lobe, controls motor functions. Contralateral motor control, initiation, planning, judgement, personality, emotions, impulsive control, Reward, social behavior, micturition, intellect, and attention. Key areas in frontal lobe are as follows. <ol style="list-style-type: none"> Premotor area (Brodman area 6) Primary motor area/cortex (4) Supplementary motor area Frontal eye field (8,9) Broca's motor speech area (44, 45) Prefrontal cortex (9,10,11,12) 		<ul style="list-style-type: none"> Lesion of prefrontal or association cortex: Frontal lobe syndrome → poor social behaviour, lack of motivation/ concentration, depression, and, anosmia Release of primitive reflexes (suckling, grasp) Lesion of Broca's area: Broca's aphasia → expressive/non-fluent type. Lesion of premotor area: Unable to perform skilful movements and inability to perform movement in sequence. Lesion of primary motor cortex/area: Paralysis of contralateral half of body Primary motor area lesion (area 4 lesion) Single limb paralysis – pure motor signs. 	
Parietal lobe	Parietal dominant (Left parietal) <ul style="list-style-type: none"> Language calculation 	Parietal non-dominant: (Right) <ul style="list-style-type: none"> Spatial orientation constructional skills (visuospatial) 	Dominant lobe lesion (Left parietal) <p>Gerstman's syndrome Features of it are:</p> <ul style="list-style-type: none"> Dysgraphia, Dyscalculia Agraphia – inability to write 	Non-Dominant lobe lesion (Right parietal) <ul style="list-style-type: none"> Constructional apraxia Or Motor apraxia. Disturbance of body image and spatial judgement Dressing apraxia Confusion Visual agnosia
Parietal lobe Processes both sensory and motor functions. (Sensory > motor). Overall, it deals with sensations, academic skills, math, reading, writing. Important areas in parietal lobes are:				

	<ol style="list-style-type: none"> Primary sensory cortex/area (3,1,2): lesion results in contralateral sensory loss, loss of tactile 2-point discrimination, touch, temperature followed by pain Recovery occurs in reverse order i.e pain recovers earliest and fine touch at the last Secondary Somesthetic area Somesthetic association area (5,7): lesion results in astereognosis. <p>For astereognosis → area 5,7 > area 3,1,2 lesion. Or Somesthetic ass. Area > 1° sensory cortex.</p>	<ul style="list-style-type: none"> ○ Alexia – unable to understand the written language ○ finger agnosia ○ right- left disorientation ○ Others: postural disturbance, tactile astereognosis ○ Contralateral inferior Quadrantanopia. ○ Tactile astereognosis ○ Postural disturbance ○ Topographic memory loss <p>For motor apraxia*: ✓ prefer parietal lobe > Premotor area. Both may cause it, but the premotor area is involved in execution of motor activity mainly. Motor apraxia is inability to do purposeful movements despite intact coordination.</p>
Temporal lobe	<p>Temporal dominant: (Left temporal)</p> <ul style="list-style-type: none"> ○ Auditory perception ○ Verbal memory ○ Speech (sensory) ○ Smell ○ balance <p>Temporal non-dominant: (Right)</p> <ul style="list-style-type: none"> ○ Music perception ○ (Melody/pitch) ○ Non-verbal memory ○ Smell ○ balance <p>Temporal lobe processes sensory inputs and special senses. Overall: speech, memory, taste, olfaction, hearing Imp areas are:</p> <ol style="list-style-type: none"> 1. Primary auditory area (41,42) 2. Secondary auditory area (22) 3. Wernicke's /sensory speech area (22) 	<ol style="list-style-type: none"> 1. Receptive (Wernicke) Fluent Aphasia: unable to understand written/spoken language. 2. Contralateral Superior Quadrantanopia (Lower Retina Involved-Meyer Loop) 3. Olfactory and Gustatory Hallucination 4. Ipsilateral Anosmia 5. Klaver Bucy Syndrome 6. Prosopagnosia
Occipital lobe	<p>Visual processing/ vision</p> <ol style="list-style-type: none"> 1. Primary visual area (17) 2. Secondary visual area (18,19) 3. Occipital eye field 	<ol style="list-style-type: none"> 1. Bilateral Lesion causes Cortical Blindness 2. Unilateral Lesion causes Contralateral Quadrantanopia 3. Macular Sparing hemianopia 4. Alexia without agraphia (vs Alexia with agraphia in parietal lobe lesion)

- **Lesion of Fusiform gyrus:** results in Prosopagnosia – inability to recognize faces.
- In Prosopagnosia: lesion of inferior temporal lobe > parieto-temporal/parieto-temporo-occipital lobe.
- Insula is buried in lateral sulcus and forms floor of lateral sulcus.
- Lesion of left insular cortex results in feeling of disgust.
- MCA supplies insula and runs in the lateral sulcus.
- Lesion of angular gyrus (area 39) may result in Grestmann's syndrome → agraphia, alexia, finger agnosia.
- Olfactory area is present in Anterior perforating substance.
- Olfactory cortex is in the inferior Temporal gyrus.

BRAIN SURFACE: LATERAL

Cerebral Cortices (Areas)

- Primary cortices**
- ✓ Initiate motor output
 - ✓ 1^o cortical sensory reception
- Association cortices**
- ✓ Process cortical information

Key Anatomical Lobes

- Cerebral lobes (4)**
- ✓ Frontal lobe (anteriorly)
 - ✓ Occipital lobe (posteriorly)
 - ✓ Temporal lobe (inferiorly)
 - ✓ Parietal lobe (borders each lobe)

LANGUAGE PRODUCTION & PROCESSING

Broca's area

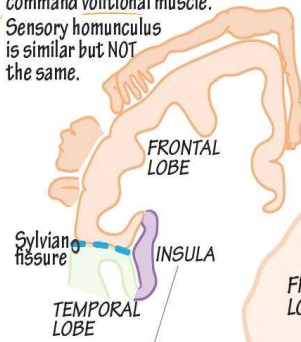
- ✓ Language output area
- ✓ Inferior frontal gyrus
- Broca's aphasia: NON-fluent aphasia

Wernicke's area

- ✓ Language reception area
- ✓ Superior temporal gyrus
- Wernicke's aphasia: Fluent aphasia

Coronal section HOMUNCULUS (MOTOR)

- ✓ Topographical dist. of neurons that command volitional muscle.
- ✓ Sensory homunculus is similar but NOT the same.



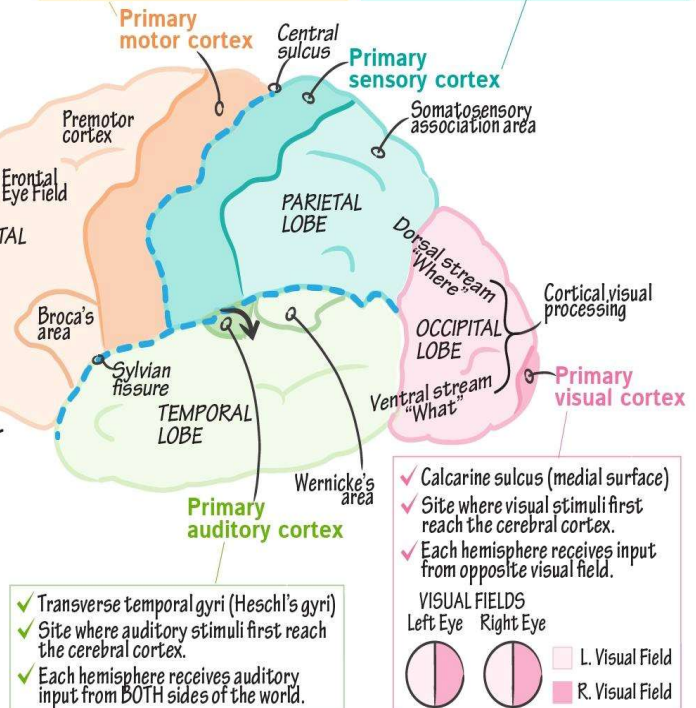
- ✓ Beneath cerebral folds
- ✓ Participates in many, varied (mostly sub-conscious) functions.

Prefrontal cortex

Lateral: Logistical
Inferior: Impulse control
Medial: Motivation

- ✓ Precentral gyrus
- ✓ Primary motor neurons in pathways that control skeletal muscle.
- ✓ Each hemisphere innervates the opposite side of the body.

Primary motor cortex



- ✓ Postcentral gyrus
- ✓ Receives sensory input from body regions that we consciously perceive.
- ✓ Each hemisphere receives sensory input from the opposite side of the body.

Primary sensory cortex

Somatosensory association area

PARIETAL LOBE

Dorsal stream "Where"

Ventral stream "What"

Occipital lobe

Primary visual cortex

Cortical visual processing

Calcarine sulcus (medial surface)

Site where visual stimuli first reach the cerebral cortex.

Each hemisphere receives input from opposite visual field.

VISUAL FIELDS

Left Eye Right Eye

L. Visual Field R. Visual Field

- ✓ Transverse temporal gyri (Heschl's gyri)
- ✓ Site where auditory stimuli first reach the cerebral cortex.
- ✓ Each hemisphere receives auditory input from BOTH sides of the world.

Primary auditory cortex

Wernicke's area

2 Parietal lobe

Dominant side

FUNCTION

Calculation
Language
Planned movement
Appreciation of size, shape, weight and texture

LESIONS

Dyscalculia
Dysphasia
Dyslexia
Apraxia
Agnosia
Homonymous hemianopia

Non-dominant side

FUNCTION

Spatial orientation
Constructional skills

LESIONS

Neglect of non-dominant side
Spatial disorientation
Constructional apraxia
Dressing apraxia
Homonymous hemianopia

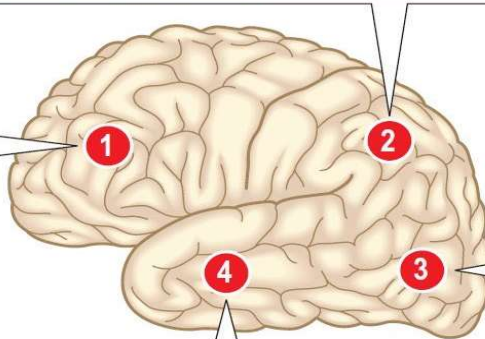
1 Frontal lobe

FUNCTION

Personality
Emotional response
Social behaviour

LESIONS

Disinhibition
Lack of initiative
Antisocial behaviour
Impaired memory
Incontinence
Grasp reflexes
Anosmia



3 Occipital lobe

FUNCTION

Analysis of vision

LESIONS

Homonymous hemianopia
Hemianopic scotomas
Visual agnosia
Impaired face recognition (prosopagnosia)
Visual hallucinations (lights, lines and zig-zags)

4 Temporal lobe

Dominant side

FUNCTION

Auditory perception
Speech, language
Verbal memory
Smell

LESIONS

Dysphasia
Dyslexia
Poor memory
Complex hallucinations (smell, sound, vision)
Homonymous hemianopia

Non-dominant side

FUNCTION

Auditory perception
Music, tone sequences
Non-verbal memory (faces, shapes, music)
Smell

LESIONS

Poor non-verbal memory
Loss of musical skills
Complex hallucinations
Homonymous hemianopia

HOMUNCULUS

- Topographical representation of motor and sensory areas in cerebral cortex.
- Distorted appearance due to certain body areas being more richly innervated have increased cortical representation. Representation is upside down.
- The finer the movement, the more representation it will have.
- Foot area is on medial most side.
- Thumb, fingers, face, and tongue cover most of the area.
- Thighs and trunk cover less area in it.
- Rest of the body including face is on lateral or Superolateral side.
- Head to toe presents from laterally to medially of cerebral hemisphere.
- HOMUNCULUS is the body's exact and opposite picture that is perceived in human head, the part of picture shown in brain controls the corresponding area of the body e.g the hand portion receives and relays info regarding hand and its opposite i.e foot is at the top and face is at the bottom of it.

SENSORY HOMUNCULUS (AREA 3,1,2)

Located in post central gyrus and sylvian fissure.
Concerned with information received via thalamus.

Largest sensory area: Lips (lower)

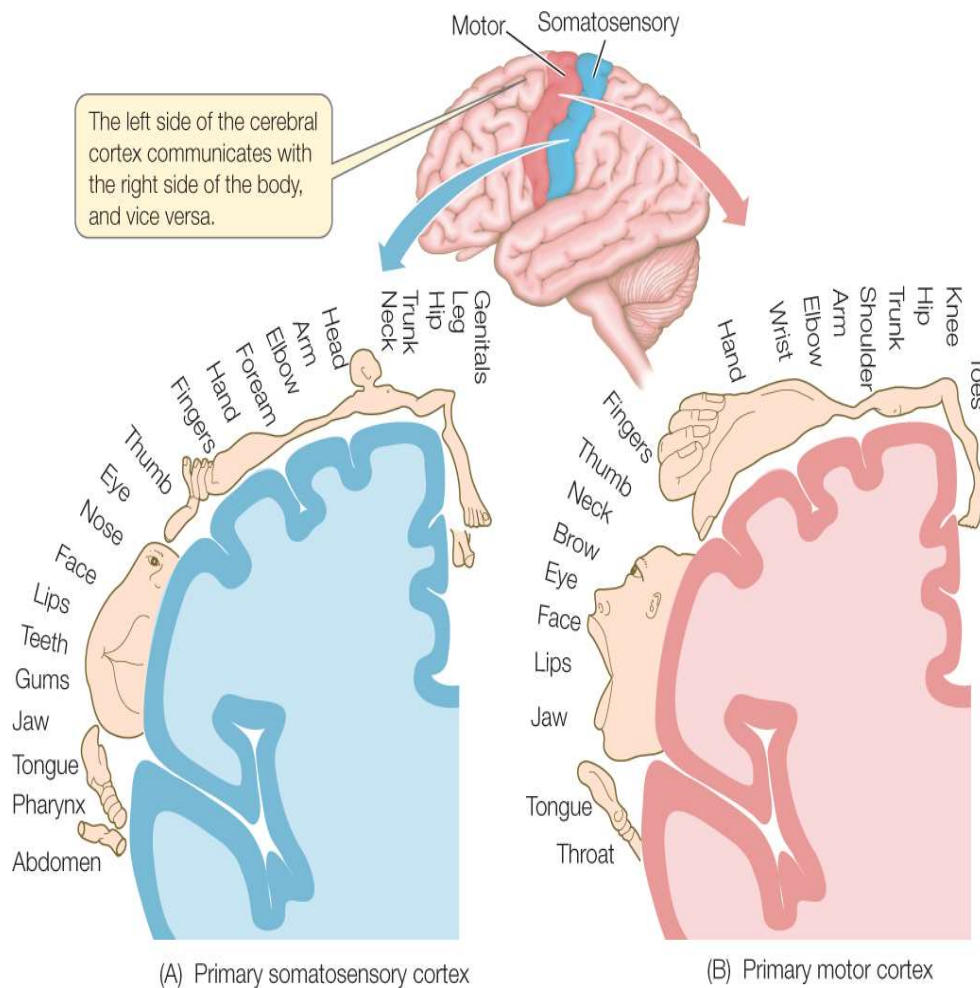
Smallest sensory area: lower limbs and trunk.

MOTOR HOMUNCULUS (AREA 4)

Located in precentral gyrus (area 4)

Concerned with information and control related to frontal lobe

- **Largest motor area:** Thumb
- **Smallest motor area:** Thigh (lower limbs) > trunk.



APHASIA

Broca's (Motor) aphasia	Wernicke's (sensory) aphasia	Conduction aphasia	Global aphasia	Anomic aphasia
Lesion of Broca's area (44,45) on inferior frontal gyrus of dominant hemisphere (Left)	Lesion of Sensory speech area 22 on superior temporal gyrus of temporal lobe.	Lesion of arcuate fasciculus that connects Wernicke to Broca's area	Broca's + Wernicke's + conduction aphasia	Lesion of Non-dominant hemisphere Broca's area + angular gyrus (39) lesion.
B = Broca & broken speech- non-fluent Comprehension and insight intact Expressive aphasia is also term used for Broca's aphasia.	Fluent aphasia or receptive aphasia, full of words, but words make no sense, poor comprehension, and lack of insight.	Poor repetition and naming Unable to conjure or put words together.	Combined effects of sensory, motor and conduction aphasia Unable to read write and speak.	Poor word retrieval or word blindness Mild Fluent aphasia Good comprehension Patients Can't express the words they want to use
Due to occlusion of MCA-superior division	Due to occlusion of MCA – inferior division	Stroke of posterior branch of MCA	Lesion of Wernicke + Broca areas and arcuate fasciculus	Associated with head trauma and Alzheimer's disease

WHITE MATTER OF BRAIN & TYPES OF FIBERS IN WHITE MATTER

Association Fibers	Commissural Fibers	Projection Fibers
Connect one gyri of same hemisphere to another gyri. Examples include. <ul style="list-style-type: none"> • Cingulum • Superior and inferior longitudinal fasciculus 	Connect the identical areas of two cerebral hemispheres. For Example: <ul style="list-style-type: none"> • Corpus callosum • Fornix (connects hippocampus to hypothalamus) • Anterior and posterior commissure • Hippocampal and Habenular commissure 	Connect the cerebral cortex to subcortical centers (corpus striatum, thalamus, brainstem) and spinal cord. <ul style="list-style-type: none"> ▪ Corticofugal fibers go from cortex to other parts of CNS. ▪ Corticopetal fibers come from other parts of CNS to cortex. Examples of Projection fibers: <ul style="list-style-type: none"> • Corona radiata + internal capsule (in Neocortex) • Optic radiation • Fimbria + fornix (in Allocortex)

CORPUS CALLOSUM (CC)

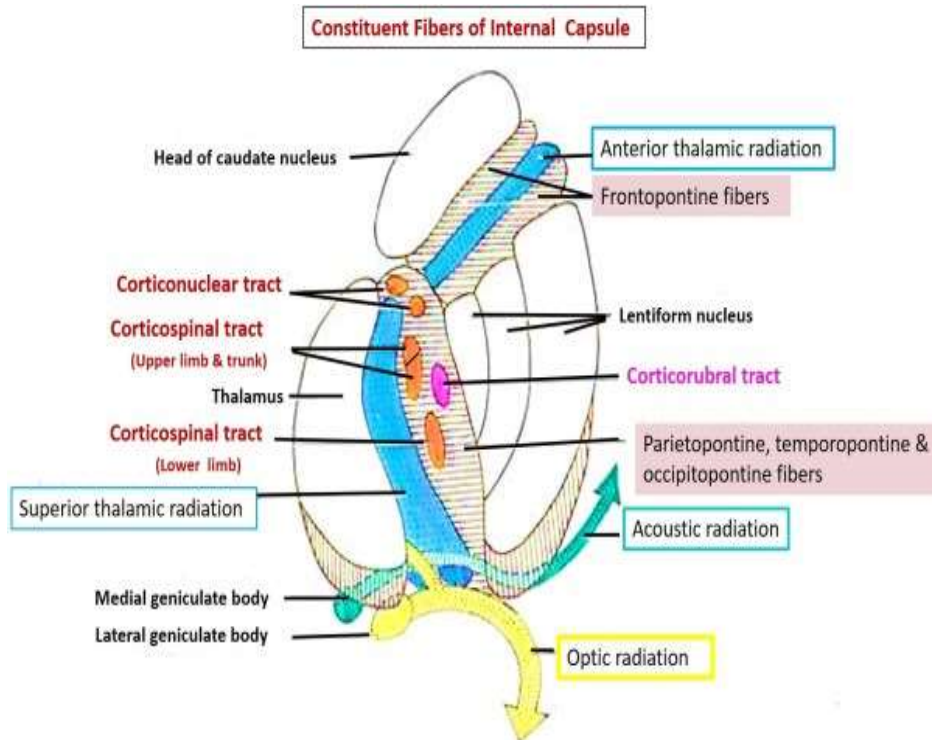
- Largest commissure consisting of 100 million fibers connecting two cerebral hemispheres for info transfer.
- In sagittal section of cerebrum, it is C shaped mass forming roof of the lateral ventricle.
- Agenesis of CC results in association loss + absence of white matter communication b/w 2 hemispheres.
- CC lesion may cause loss of communication b/w 2 lobes of hemispheres and transcortical apraxia.
- It is divided from backwards into 4 parts: Genu, rostrum, trunk, and splenium.

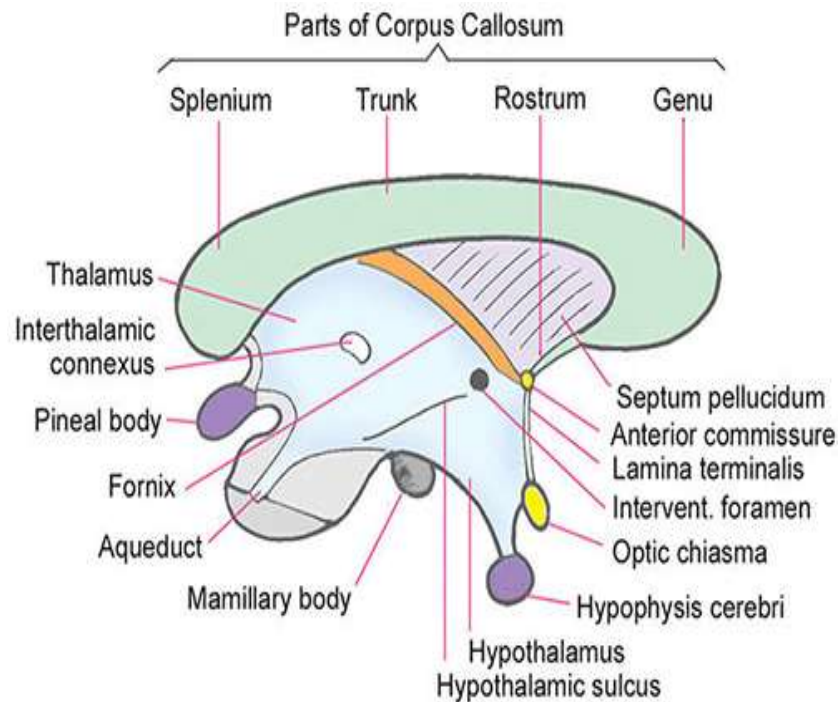
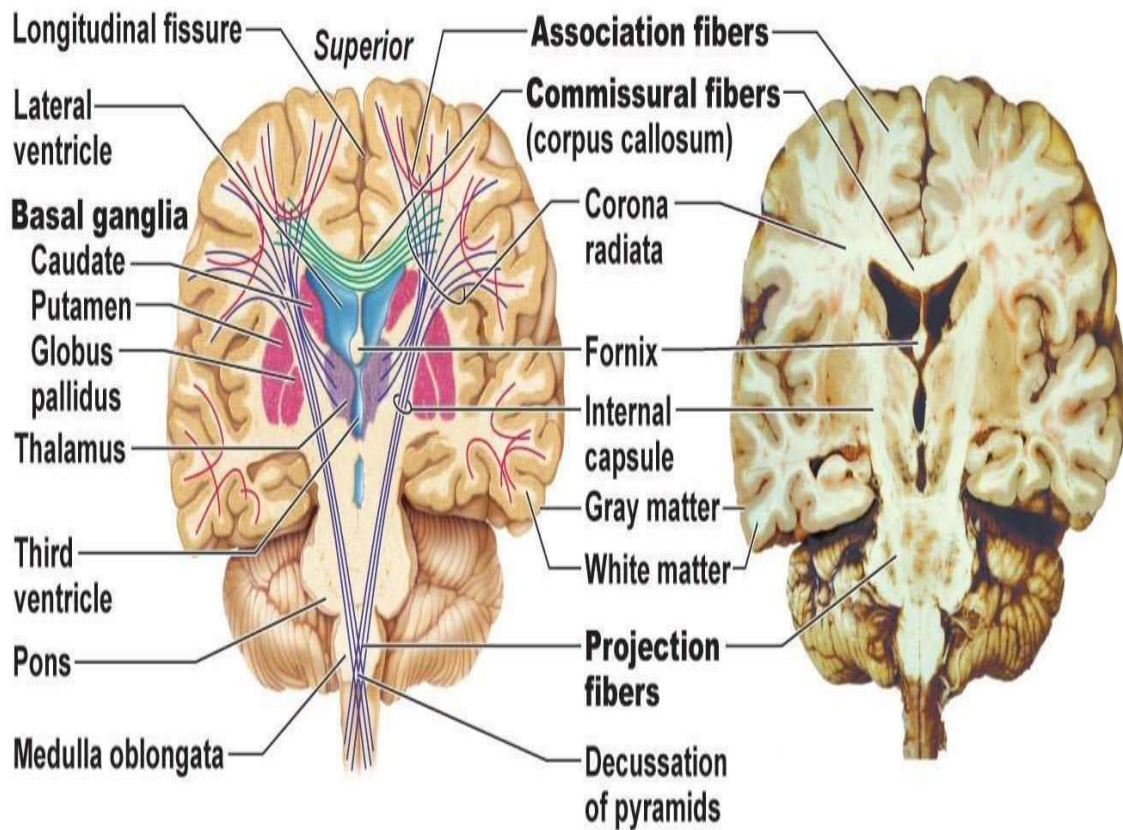
Genu	Rostrum	Trunk	Splenium
Fork like thick anterior end Forceps minor connects the frontal lobes for coordination of sensory and motor information.	Gene extends downwards and backward to join lamina terminals, forming rostrum that connects orbital surfaces of frontal lobes.	Main part of CC b/w its thick anterior genu and massive posterior splenium.	Massive posterior part lying in front of occipital pole. The fibres of splenium or connect parietal, temporal and occipital lobes. Forceps major are the fibers connecting occipital and parietal lobes, sweep on either side above Calcarine sulcus forming fork like structure.

INTERNAL CAPSULE

- V - shaped bunch of White matter projection fibers composed of ascending and descending nerve Fibers that connect the Cerebral cortex to the brainstem and spinal cord.
- Parts include an anterior limb, genu, posterior limb, retrolentiform and sub Lentiform parts.

Relations	Components		Blood supply
<ul style="list-style-type: none"> • Medial Side The tailed shaped Caudate Nucleus and Thalamus • Lateral Side A Lens Shaped Lentiform nucleus. Lentiform= Putamen + Globus Pallidus (mnemonics = LPG) 	Part	Carries fibers	<p>From both MCA + ACA Main supply: MCA</p> <p>■ Genu + post. Limb: supplied by MCA via lenticulostriate branches.</p> <p>■ Anterior limb supplied by (MCA+ACA) MCA – lateral striatal branches (Charcoat's artery) ACA – recurrent branch known as Heubner's artery.</p> <p>■ Sub lentiform + retro Lentiform both are supplied by these 2: Posterior cerebral artery Anterior choroidal artery</p>
	Anterior limb	<ul style="list-style-type: none"> ▪ Corticopontine fibers ▪ Papez circuit of limbic system ▪ Anterior thalamic radiations 	
	Genu	<ul style="list-style-type: none"> ▪ Corticonuclear and corticospinal fibers for head and neck. ▪ Superior thalamic radiations 	
	Posterior limb	<p>Anterior 2/3rd: it has motor fibers that control all skeletal muscles of the body. It has</p> <ul style="list-style-type: none"> ▪ Corticopontine fibers ▪ Corticospinal fibers for upper, lower limbs + trunk. <p>Posterior 1/3rd: it has sensory fibers.</p> <ul style="list-style-type: none"> ▪ Superior thalamic radiations ▪ Most posterior in post. Limb are Optic radiation fibers 	
	Retrolentiform	<ul style="list-style-type: none"> ▪ Corticopontine fiber ▪ Optic radiations (posterior thalamic radiations) 	
	Sublentiform	<ul style="list-style-type: none"> ▪ Auditory radiations (inferior thalamic radiations) 	





BASAL GANGLIA

- Large cortical masses of gray matter situated inside the white matter of cerebrum, consisting of striatum, globus pallidus, subthalamic nuclei and functionally includes substantia nigra + Red nucleus also.
- Corpus striatum = Caudate nucleus + Lentiform Nucleus (CCL – Caribbean cricket league)
- Neostriatum = Caudate nucleus + putamen (NCP)
- Lentiform nucleus = Putamen (lateral) + Globus pallidus (Medial part lateral to internal capsule) = LPG
- Caudate is a C shaped mass of gray matter lying lateral to thalamus and medial to internal capsule
It has a head, body, and tail. Amygdala (part of limbic system) is attached to tail of caudate
- Globus pallidus is divided into external (Gpe) and internal segments (Gi).
- Basal ganglia have high O₂ consumption rate and **high Copper content**.
- **BG** is separated from thalamus by posterior limb of internal capsule.
- **Blood supply of BG is by Middle cerebral artery – lenticulostriate branches.**
- Afferents via corticostriate + thalamostriatal pathway using Glutamate (excitatory) neurotransmitter.
- The 2 major outputs of basal ganglia are from Gpi and substantia nigra pars reticulata → both inhibitory.
- Neurotransmitter in basal ganglia outflow pathway (inhibitory) is GABA.
- The striatum communicates with thalamus and cerebral cortex by opposing pathways using Dopamine.
- 1. **Dopamine inhibits the Indirect pathway via D₂ receptors. So, Indirect pathway is overall → inhibitory.**
- 2. **Dopamine stimulates the Direct pathway via D₁ receptors. So, direct pathway is overall → excitatory.**
Via stimulation of stimulatory pathway and inhibition of inhibitory pathway dopamine is → Excitatory.

Direct (Excitatory pathway)	Indirect (Inhibitory pathway)
Substantia nigra (SNc) input to the striatum via nigrostriatal dopaminergic pathway releases GABA which inhibits the GABA released from Gpi, disinhibiting the thalamus via the GPI (↑ motion) Lesion of direct pathway → hyperkinesia	SNc input to the striatum via nigrostriatal dopaminergic pathway releases GABA that disinhibits subthalamic nuclei (STN) via Gpe inhibition, and STN stimulates Gpi to inhibit the thalamus (↓ motion) Lesion of indirect pathway → hypo kinesis

- **Basic circuit: Cortex → + striatum → - pallidum → - thalamus → + cortex**
- Receive input from cortex and return it back to cortex (**cortico-striato-pallido-thalamo-cortical loop**).
- All connections of basal ganglia are with ipsilateral cortex.

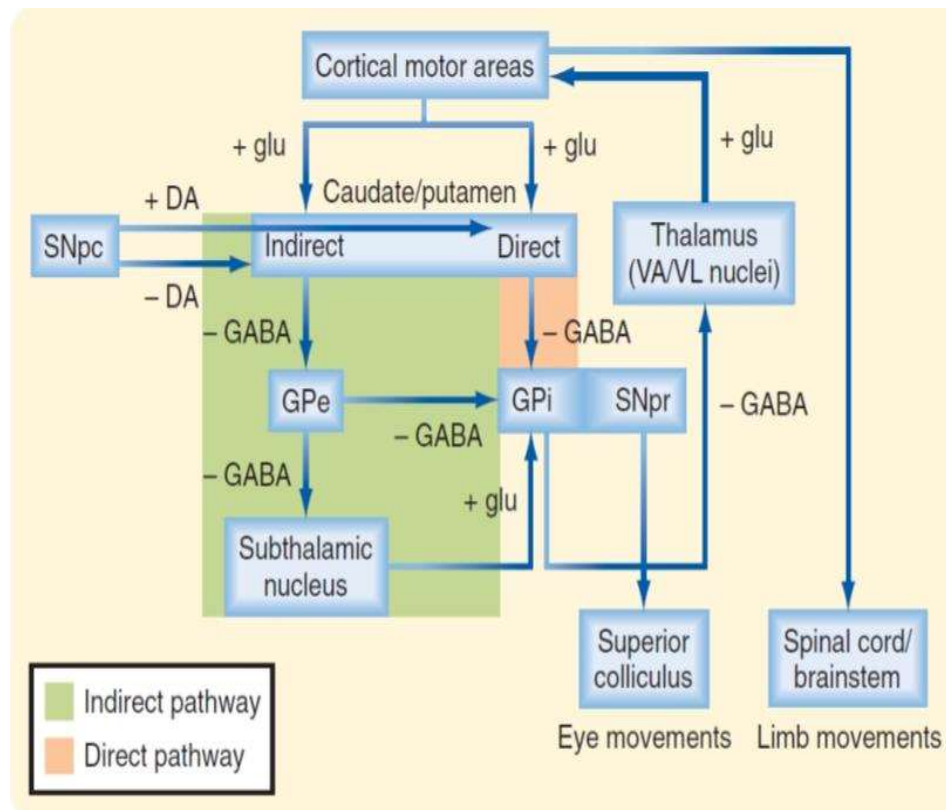
Substantia Nigra (SNc) is the largest nucleus of midbrain, divided into pars compacta + pars reticulata and situated between tegmentum and crus cerebri. Its lesion occurs in Parkinson's disease.

Functions of Basal Ganglia:

1. Basal ganglia modulate thalamic outflow to the motor cortex **to initiate, plan and execute smooth movements**.
2. Starting and stopping voluntary movement and inhibiting unwanted movements.
3. Initiation + gross control of skeletal muscle movement.
4. Caudate deals with cognitive (thinking) functions
5. Putamen participates in the subconscious performance of learned pattern of skilled movements. E.g cutting a paper.
6. Globus pallidus help girdle movements or lock the movements.

Part Of BG	Effect Of Lesion
Striatum	Chorea → Quick, continuous, purposeless involuntary jerky/flicking movements in hands, face, or other body parts e.g Huntington's chorea due to atrophy of caudate + putamen.
Globus pallidus	Athetosis → spontaneous slow writhing (worm like) movements of hands, face, or neck due to lesion of globus pallidus. Inability to maintain posture may occur in GP lesions.
Subthalamic nucleus	Hemiballismus → sudden wild flailing/flinging movements of entire limb caused by lesion of contralateral STN.
Substantia nigra	Parkinson's disease → due to destruction of dopaminergic neurons in substantia nigra pars compacta results in rigidity (lead pipe + cogwheel type), reduced voluntary movements (bradykinesia), flat facies (mask like), pill rolling tremors, stooped posture and shuffling gait.
Lentiform nucleus	Wilson's disease: hepatolenticular degeneration due to copper deposition in globus pallidus and putamen nucleus.

- Clasp knife rigidity is seen in UMNL whereas Cogwheel or lead pipe rigidity present in basal ganglia lesion
- Drugs given to abolish rigidity are chlorpromazine, Ropinirole, pramipexole (in Parkinsonism)
- Carbidopa + Levodopa is well tolerated in Parkinson's disease.



LIMBIC SYSTEM (LIMBIC LOBE)

- Collection of forebrain neural structures involved in emotions, long-term memory and olfaction, behavioral modulations, and, autonomic functions.
- Limbic system comprises of Amygdala, Hippocampus, cingulate gyrus, mammillary bodies, anterior thalamic nuclei, and entorhinal cortex, all these collectively responsible for **feeding, fleeing, fighting, feeling and sex (5 F's)**
- Hippocampus stores long term memories. Lesion may result in anterograde amnesia-inability to form new memories.
- Feeding, chewing, licking and emotions (fear, rage) is by amygdala.
- Learning and emotional behaviour, motivational (reward and punishment) is dealt by this system.

Papez Circuit (Memory processing):

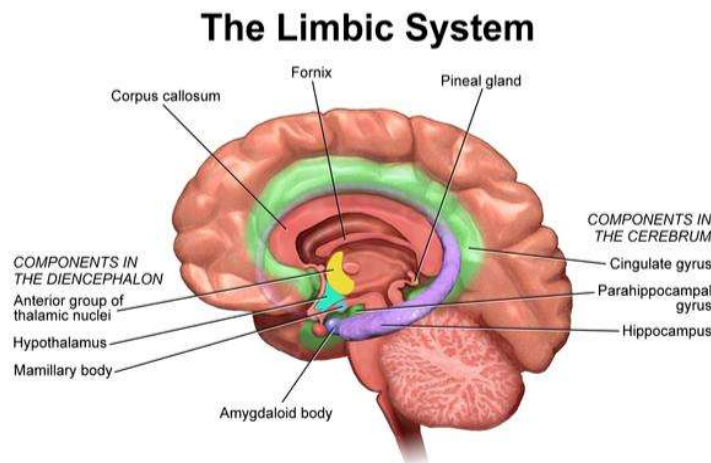
- Axons of hippocampal pyramidal cells converge to form the fimbria and, finally, the fornix, The Fornix projects to the mammillary bodies in hypothalamus. The mammillary bodies project to the anterior nucleus of the thalamus (mammillo-thalamic tract). The anterior nuclei project to the Cingulate gyrus, and the cingulate gyrus projects to the entorhinal cortex (via the cingulum). The Entorhinal cortex projects to the hippocampus (via the perforant pathway).
- **Entorhinal cortex → Hippocampus → mammillary bodies → anterior thalamic nuclei → cingulate gyrus → Entorhinal cortex.**
- **Perforant pathway:** dentate gyrus → CA3 → CA1 → Subiculum (Hippocampus). CA3 & CA1 are areas in hippocampus for rapid decoding of memory.

Lesion of Bilateral Temporal lobe – (Amygdala + Hippocampus -- Kluver Bucy syndrome):

- Features include hyper orality + hypersexuality, decreased emotions/Placidity (decreased fear and rage), visual agnosia or psychic blindness, anterograde amnesia and hypermetamorphosis (visual stimulus are repeatedly approached as they are newer ones).

Lesion of Mammillary Bodies – Korsakoff syndrome:

- Seen in chronic alcoholics who are thiamine (Vit B1) deficient due to necrosis of mammillary bodies.
- Anterograde > Retrograde amnesia occurs.
- Patients confabulate memories - generate stories to cover gap of memory.
- **Retrograde amnesia:** inability to remember things that occurred before CNS insult i.e can't recall memories but can generate new memories.
- Past memories can be recalled by repeatedly exposing to those events.
- **Anterograde amnesia:** inability to remember things that occurred after CNS insult, can recall past memories but cannot generate new memories.



Diencephalon

- The cavity within it is the third ventricle. Diencephalon is divided into pars dorsalis and pars ventralis.
- Pars dorsalis → thalamus (dorsal thalamus), metathalamus, and epithalamus
- Pars ventralis → Hypothalamus, subthalamus (ventral thalamus).
- Metathalamus contains medial + lateral geniculate bodies.
- Epithalamus contains the Pineal gland + Habenular nuclei.

THALAMUS

- Largest diencephalic ovoid mass of grey matter which acts as major relay station for all sensory information except olfaction and acts as afferent gateway of cerebral cortex including somatosensory information, sleep and arousal, recent memory, genesis of EEG, perception of sexual sensations, maintaining consciousness and alert responses.
- It is divided by internal medullary lamina into lateral, medial, and anterior nuclear masses.
- Two thalami lie close together in cephalic 2/3rd and separated by lateral ventricles.
- Thalamus is supplied by **Posterior cerebral artery + posterior communicating artery**.
- Anatomical classification of nuclei of thalamus with their significant role is given in table below.

NUCLEI	FUNCTIONS
1. Anterior Group a. Ant ventral b. Ant dorsal c. Ant medial	Anterior nuclear group → part of Papez circuit, important for recent memory and emotions. Dorsomedial nucleus → most important nucleus, role of fear, fright, and memory (damaged in Wernicke's Korsakoff syndrome). Regulates emotions, feelings, and olfactory information. Medial geniculate bodies : mass of thalamus, lies on midbrain. Perceives Auditory information via superior olivary nucleus + inferior colliculus of tectum. Lateral geniculate bodies receive Vision related information.
2. Medial group a. Centro median b. Dorso median c. Midline dorsal	Ventral postero- medial (VPM) : receives input from trigeminal + gustatory pathway, carries sensations from face + taste sensations and transmits them to 1° sensory cortex in parietal lobe. Ventral postero- lateral nucleus (VPL) : receives pain, temperature, pressure, vibration, light touch via Spinothalamic and dorsal column medial lemniscus system → sends to primary sensory cortex. Ventral anterior and lateral nucleus (VAN) : receives motor input from basal ganglia + cerebellum and transfers to the frontal lobe. Midline + interlaminar nuclei are important in mediating EEG desynchronization during arousal. <ul style="list-style-type: none"> • From Postero-medial/lateral nuclei information goes to → Parietal lobe (P – P) • From ventral anterior, information goes to → frontal lobe (as frontal lobe is anterior + motor)
3. Lateral group a. Dorsal Group : pulvinar, lateral dorsal, lateral posterior nucleus b. Ventral group : ventral posterior, ventral anterior, ventral medial, medial, and lateral geniculate bodies	

Thalamic syndrome (Dejerine Roussy syndrome)

- ❖ Due to lesion /blockade of Posterior cerebral artery (thalamogeniculate branch) in stroke, hemorrhage, or trauma.
- ❖ Affected nucleus are mainly postero lateral and postero medial.
- ❖ Sensory + motor loss occurs on contralateral side.
- ❖ Loss of tactile localization, tactile discrimination, touch, grade of temperature on contralateral side.
- ❖ Exaggeration of pain sensation (pin prick felt as bullet) that is unresponsive to analgesics.
- ❖ Loss of recent memory or emotions.
- ❖ Hypotonia, weakness and ataxia due to damage of cerebellothalamic tract.
- ❖ Astereognosis and amelognosis (illusion of absent limb)
- ❖ Ataxia, chorea and Athetosis due to damage of connection between thalamus and basal ganglia.
- ❖ Thalamic hand/athetoid hand: moderate wrist flexion and hyperextended fingers.
- ❖ Thalamic phantom limb: unable to locate position of limb on closed eye due to loss of joint position sensation.

- ❖ Thalamic pain syndrome occurs in patients recovering from stroke (8% cases), affects ventral nuclear group, threshold for pain, temperature, and, touch is decreased on opposite side of the body.
- ❖ Patient is aroused by light touch or cold and fails to respond to strong analgesic agents.
- ❖ Frontal lobotomy may be done to relieve intractable pain, dividing dorsal thalamic nuclei from frontal lobe.

PINEAL GLAND

- A cone shaped reddish -grey neuroendocrine gland present b/w the two superior colliculi.
- Pineal gland is present in midline, outside blood-brain barrier and attached to roof of third ventricle via short stalk. It has pinealocytes (secrete melatonin) and neuroglial cells
- Melatonin levels rise in the dark.
- It regulates circadian rhythm (biological clock) and inhibits GnRh release from hypothalamus.
- Due to the ability to regulate circadian rhythm with light pineal gland is also known as the third eye.
- Secretion of melatonin is regulated by hypothalamus via post-ganglionic fibers which secrete epinephrine.
- All parts of brain have neural cells except pineal gland.
- It is the only part of brain supplied by nerve arising outside the brain, the nervus conarii.
- It was also regarded as the seat of soul due to previous assumptions that it is the only mobile structure in brain.
- Disorders of pineal gland may result in precocious puberty, insomnia, Parinaud syndrome, and, hydrocephalus (due to obstruction to CSF flow or over production).
- Defect in pineal gland causes: insomnia > Precocious puberty.
- If the Q is like this → defect in pineal gland results in dec. Melatonin, it may lead to: Early puberty.
- Circadian rhythm is controlled by Suprachiasmatic nucleus of hypothalamus > Epithalamus (Pineal gland)

HYPOTHALAMUS

- Medial most part of diencephalon situated in lateral wall and floor of 3rd ventricle below the thalamus, 4gm in weight and extends from 3rd ventricle to mammillary bodies.
- Below it lies the base of brain, laterally internal capsule and medially the third ventricle.
- **Functions of Hypothalamus** are following: (Mnemonics = AS -RESPECT)
 - Autonomic functions,
 - Sleep -wake cycle,
 - Reward & punishment Centre,
 - Endocrinal functions,
 - Sexual behaviour & Reproduction,
 - Ph(F) food intake Regulation,
 - Emotional & Instinctual Behaviour,
 - Circadian Rhythm Control, and
 - Temperature regulation.
- Hormones secreted by it include the trophic factors i.e TRH, CRH, GHRH, GHIH, Dopamine, Prolactin releasing factor, GnRh.
- Hypothalamic hypophyseal system arises in the Medial hypothalamus.
- Arcuate nucleus has neurons for secreting prolactin.
- Reward center is lateral + Dorso medial nucleus.
- Punishment center = Medial nucleus.

Nuclei	Functions	Remarks
Lateral	<ul style="list-style-type: none"> Role in Hunger Destruction may lead to anorexia. Hunger is stimulated by Ghrelin, neuropeptides Y, orexins A, B and MCH. Hunger is inhibited by leptin 	<ul style="list-style-type: none"> Lateral lesion makes you lean. Ghrelin helps in gaining weight (G-G) Leptin helps you losing weight (L-L)
Ventromedial	<ul style="list-style-type: none"> Role in mediating satiety (satiety center) Lesion of VMN may result in hyperphagia (obese) 	<ul style="list-style-type: none"> Leptin stimulates this center. Medial lesion makes you → Massive
Anterior	<ul style="list-style-type: none"> Cooling center, parasympathetic action. Activates sweating in response to elevated temperature. 	<ul style="list-style-type: none"> AC = Anterior – cooling
Posterior	<ul style="list-style-type: none"> Heating center, sympathetic action Activates shivering thermogenesis mechanism 	<ul style="list-style-type: none"> Hot Pot = Heating - Posterior
Suprachiasmatic	<ul style="list-style-type: none"> Regulates circadian rhythm by direct retinal input 	<ul style="list-style-type: none"> SC = Suprachiasmatic – circadian
Supra optic	<ul style="list-style-type: none"> Synthesizes ADH 	<ul style="list-style-type: none"> Both hormones are carried by neurophysins to posterior pituitary. Hormones are stored in nerve endings.
Paraventricular	<ul style="list-style-type: none"> Synthesized Oxytocin 	
Preoptic	<ul style="list-style-type: none"> Releases GnRh. mediates sexual behaviour. Overall thermoregulation control. 	<ul style="list-style-type: none"> Failure of GnRh producing neurons to migrate from olfactory pit → Kalman syndrome

Temperature Regulation (Concept of Heat Gain & Heat Loss)

Heat Gain (Hyperthermia)

- Posterior Hypothalamus** is activated by Cold → activates Sympathetic system which will increase Heating by cutaneous vasoconstriction and Shivering. **Shivering is the most potent mechanism for heat generation.** Most immediate response to cold is catecholamines mediated vasoconstriction. It also increases hunger.
- During shivering thermogenesis **uncoupling of oxidative phosphorylation is done by:**
Nor-epinephrine > thyroxine.

Heat Loss (Cold / Poikilothermia)

Anterior Hypothalamus is activated via hot temperature → activates parasympathetic system that will increase Cooling by **Vasodilation** and **sweating**.
Vasodilation is the 1st physiological response to high temperature.

- Overall Temperature regulation **Preoptic Nucleus > Anterior Hypothalamus**

Summary:

CSP = Cold - Sympathetic - Posterior hypothalamus

- Cold** → + posterior hypothalamus → + sympathetic system → vasoconstriction + shivering → **↑** Heat/temp
- Heat** → + anterior hypothalamus → + parasympathetic system → vasodilation + sweating → cooling/ **↓** temp

Important Concept

- Pyrogens increase the set point temperature of hypothalamus via IL – 1 which inc. The production of PGE2. PGE2 inc. The set point temp, so the core body temperature will now be recognized as lower than normal, thus heat generating mechanism will be activated that result in increased body temperature and fever
- If set point temp is inc → there will be inc shivering and dec. Sweating, as occurs in fever.
- If set point temp is dec → there will be inc sweating and dec. Shivering
- Normal body temp is 37.6 C (98.6 F), hyperthermia → $\geq 41^{\circ}\text{C}$ (106 F°), Hypothermia → $\leq 35^{\circ}\text{C}$ (95F°)
- Malignant hyperthermia occurs due to mutation of ryanodine R1 receptors, as a side effect of inhalational anaesthetic agents/ succinylcholine. Heat is generated via skeletal muscle contraction.

SLEEP

- Sleep cycle is regulated by the circadian rhythm, which is driven by Suprachiasmatic nucleus (SCN) of the hypothalamus.
- Circadian rhythm controls nocturnal release of ACTH, prolactin, Melatonin and Norepinephrine.
- SCN → norepinephrine released → pineal gland → ↑ Melatonin.
- SCN is regulated by environment (e.g, light)
- Two stages of sleep are rapid-eye movement (REM 25% of sleep) and non-REM (75% of sleep)
- Loss of muscle tone occurs in REM and loss of vascular tone is a feature of NREM.
- Alcohol, benzodiazepines, and barbiturates are associated with ↓ REM sleep and N3 sleep
- Norepinephrine also ↓ REM sleep
- Benzodiazepines are useful for night terrors and sleepwalking by ↓ N3 and REM sleep
- Anterior hypothalamus is facilitatory for sleep and posterior hypothalamus is inhibitory (for awake).
- Energy during sleep is NOT derived by loss of skeletal muscle tone.
- Awake with eyes open → beta waves (highest frequency, lowest amplitude) – active mental concentration e.g while solving a math problem or scenario.
- Awake with eyes closed → Alpha waves

Stages of Sleep & Associated EEG Waveforms									
Rapid eye movement (REM) 25%	Non-rapid eye movement (NREM) 75%								
<ol style="list-style-type: none"> 1. REM sleep centre is locus coeruleus (Pons) and neurotransmitter is Acetylcholine. 2. It occurs every 90 minutes (4 – 6 cycles/night) and duration increases throughout night. 3. Beta waves appear on EEG (highest frequency 14 -80 HZ) 4. Dreams occur frequently here and may be recalled. 5. REM is 80% in premature infants, 50% in neonates and 25% in adults. <p>REM is linked with marked brain activity and the individual is difficult to arouse while sleeping, so REM is also called paradoxical sleep.</p> <p>Desynchronized sleep is also a term used for REM due to lack in synchrony of neuronal firing.</p> <p>Features of REM</p> <ul style="list-style-type: none"> • Loss of motor tone and Variable pulse, B.P • ↑ O₂ consumption by brain, inc eye movement due to paramedian pontine reticular formation • Nightmares occur (not night terror) • Penile erection/ clitoral tumescence • Pupil constriction 	<ol style="list-style-type: none"> 1. NREM sleep center is Raphe nucleus of brain stem and neurotransmitter are Serotonin > GABA. 2. NREM is also called slow wave sleep, has 4 stages N1, N2, N3 ad N4 3. EEG waveforms include theta waves (N1), sleep spindles and K complexes (N2) and delta waves (N3) 4. Dreams may occur but cannot be recalled. 5. N1 is 5%, N2 45%, N3 25% (deepest sleep). <table border="1"> <tr> <td>N1</td><td>5%, Light sleep and theta waves appear on EEG. Theta waves also appear in stress (4 – 7 Hz)</td></tr> <tr> <td>N2</td><td>45%, deeper sleep, tooth grinding (Bruxism) occurs. Sleep spindles & K complexes (high voltage biphasic waves) appear on EEG. Spindles may occur in N1, but mainly in N2.</td></tr> <tr> <td>N3</td><td>25%, Deepest non- REM sleep, Sleepwalking, sleep talking, night terrors and bed wetting occurs here. Loss of vascular tone is also an important feature. Delta waves – lowest frequency and highest amplitude occur here (0.5 – 4 Hz). They also appear in infancy and organic brain disease</td></tr> <tr> <td>N4</td><td>Maximum slowing here, delta waves appear.</td></tr> </table> <p>Remember that night terrors in NREM (N3) and nightmares in REM sleep. Sleepwalking, talking → N3</p>	N1	5%, Light sleep and theta waves appear on EEG. Theta waves also appear in stress (4 – 7 Hz)	N2	45%, deeper sleep, tooth grinding (Bruxism) occurs. Sleep spindles & K complexes (high voltage biphasic waves) appear on EEG. Spindles may occur in N1, but mainly in N2.	N3	25%, Deepest non- REM sleep, Sleepwalking, sleep talking, night terrors and bed wetting occurs here. Loss of vascular tone is also an important feature. Delta waves – lowest frequency and highest amplitude occur here (0.5 – 4 Hz). They also appear in infancy and organic brain disease	N4	Maximum slowing here, delta waves appear.
N1	5%, Light sleep and theta waves appear on EEG. Theta waves also appear in stress (4 – 7 Hz)								
N2	45%, deeper sleep, tooth grinding (Bruxism) occurs. Sleep spindles & K complexes (high voltage biphasic waves) appear on EEG. Spindles may occur in N1, but mainly in N2.								
N3	25%, Deepest non- REM sleep, Sleepwalking, sleep talking, night terrors and bed wetting occurs here. Loss of vascular tone is also an important feature. Delta waves – lowest frequency and highest amplitude occur here (0.5 – 4 Hz). They also appear in infancy and organic brain disease								
N4	Maximum slowing here, delta waves appear.								
Changes in Elderly	↓ REM sleep time ↓ N3 ↑ sleep latency, ↑ early awakenings								
Changes in Depression	Terminal insomnia, repeated night-time awakening, early morning awakening.								
Narcolepsy	↓ N3 + REM latency, ↑ REM time								
	Only ↓ REM latency								

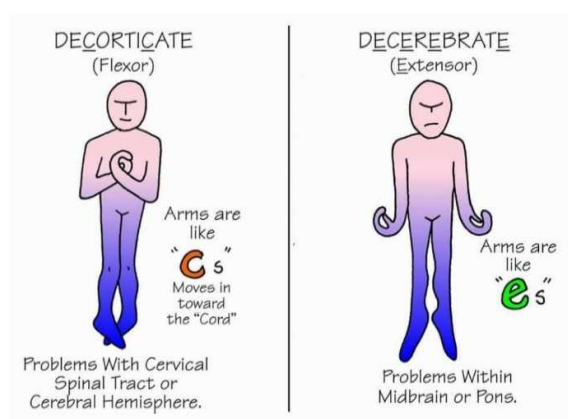
BRAIN STEM

(From below upwards, it consists of medulla oblongata, pons, and the mid brain)

Medulla Oblongata	Pons	Midbrain
<p>Direct continuation of spinal cord extending from foramen magnum to pons.</p> <p>Upper part of medulla has relation with 4th ventricle posteriorly. Open part of medulla forms the lower part of floor of fourth ventricle.</p> <p>Medulla contains vital centers: respiratory, swallowing, vomiting and vasomotor.</p> <p>On ventral aspect of medulla, Pyramids and olives are present. These are key distinguishing features.</p> <p>■ Pyramids in inferior medulla are elevations formed by underlying corticospinal or pyramidal fibers.</p> <p>Lesion of pyramid causes → motor loss</p> <p>■ Olives in upper half of medulla are formed due to underlying inferior olivary nucleus.</p> <p>Medulla contains CN nuclei of 9,10,11,12 CN.</p> <p>Inferior cerebellar peduncle connects medulla to cerebellum.</p>	<p>Largest part of brain stem present b/w medulla and midbrain.</p> <p>On either side, pons continues as middle cerebellar peduncle.</p> <p>Ventral aspect has a basilar groove for basilar artery</p> <p>Junction between midbrain and pons is marked by cerebral peduncles.</p> <p>Cavity of pons: 4th ventricle.</p> <p>CN 5,6,7, 8 nuclei are present in pons.</p> <p>Ponto-medullary junctions contains from medial to lateral:</p> <p>CN 6 – Abducent nerve</p> <p>CN 7 – Facial nerve</p> <p>CN 8 – Vestibulocochlear nerve</p> <p>Facial colliculus passes through lower dorsal pons, formed by looping of CN7 around CN6.</p> <p>Trigeminal nucleus is the main sensory and motor nucleus of CN5 passed through upper pons.</p> <p>Trapezoid body is present in caudal pons, receives auditory fibers from cochlear nuclei. They decussate here/cross midline.</p>	<p>Shortest part of brain stem</p> <p>Cavity: cerebral aqueduct connects 3rd Vent with 4th.</p> <p>Substantia nigra is the largest nucleus of midbrain.</p> <p>Midbrain consists of tectum, tegmentum, and crus cerebri.</p> <p>CN3 and CN 4 nuclei present in midbrain.</p> <p>On dorsal aspect: superior and inferior colliculus seen</p> <p>Superior colliculus: Visual reflex centre, CN 3 present at this level.</p> <p>Inferior colliculus: Auditory reflex center, CN 4 present at this level.</p> <p>Superior brachium connects the superior colliculus to lateral geniculate body and optic tract (has optic fibers).</p> <p>Inferior brachium connects the inferior colliculus to medial geniculate body and made of auditory fibers.</p> <p>Only CN to arise on posterior or dorsal side of brain: trochlear nerve CN4</p> <p>Tectum of midbrain deals with light reflex</p>

Part of Medulla	Nucleus present
Upper medulla	<ul style="list-style-type: none"> Inferior olivary nucleus vestibulocochlear nucleus spinal trigeminal nucleus
Middle medulla	<ul style="list-style-type: none"> Nucleus ambiguus – central Dorsal vagal nucleus Hypoglossal nucleus Spinal trigeminal nucleus
Lower medulla	<ul style="list-style-type: none"> Dorsal vagal nucleus Hypoglossal nucleus Spinal trigeminal nucleus

Decorticate rigidity	Decerebrate rigidity
<ol style="list-style-type: none"> 1. Transaction at superior colliculus level or lesion above red nucleus of midbrain, worse prognosis. 2. Increased flexor tone in all 4 limbs 	<ol style="list-style-type: none"> 3. Transaction at Mid-collicular level or lesion at or below red nucleus leads to extensor posturing. 1. Increased extensor tone in all 4 limbs



RETICULAR FORMATION

- Cluster of neurons and nerve cells present along entire length of brain stem, extending cranially to diencephalon and caudally to spinal cord.
- Depending on modalities some sensations pass through it while others bypass it.
- It is divided into ascending and descending reticular activating system.
- **Ascending reticular activating system** is more discrete in the floor of cerebral aqueduct.
- It is believed to be responsible for maintenance of alertness and consciousness of the brain – simply termed as **reticular activating system**.
- Acetylcholine plays key role as an excitatory neurotransmitter in this process. Unusual stimulus causes arousal.
- **Descending reticular activating system** consists of pathways to autonomic centers of brainstem regulating the functions of vital centers → respiratory, cardiac, and, vasomotor centers.

CRANIAL NERVE NUCLEI

- Located in tegmentum portion of brain stem (between dorsal and ventral portions).
- Lateral nuclei are sensory (arise from alar plate) and medial nuclei are motor (arise from basal plate).
- 4 CN are above pons (1,2,3,4), 4 CN exit the pons (5,6,7,8) and 4 are in medulla (9,10,11,12).
- 4 CN nuclei are medial → 3, 4, 6, 12 (factor of 12, except 1 and 2).
- In Cavernous sinus thrombosis first CN to be affected is Abducent nerve – CN 6 (present in center/median).
- Lesions of medulla oblongata involves hypoglossal nerve mostly – CN12 (medial structure).

Nucleus	Contains CN	Functions
Nucleus tractus solitarius	7, 9, 10 NTS = nine, ten, seven	Role in vomiting + visceral sensory information → taste, baroreceptors, and gut distension. NTS for Taste.
Nucleus ambiguus	9, 10, 11	Swallowing + palate elevation by supplying motor innervation to muscles of pharynx, larynx, and upper Esophagus.
Dorsal motor nucleus	10 th CN only	Sends autonomic (parasympathetic) fibers to heart, lungs, and upper GIT

CRANIAL NERVE REFLEXES

Reflex	Corneal	Pupillary	Cough	Gag	Jaw jerk	Lacrimation
Afferent	Nasociliary branch of ophthalmic (V1)	CN II	CN X	CN. IX	Mandibular nerve (V3) Sensory branch	Ophthalmic nerve V1
Efferent	Temporal branch of facial nerve.	CN III	CNX	CN X	Mandibular nerve (V3) Motor – masseter muscle	CN VII (facial nerve)

- **Tongue and Jaw deviate towards the site of lesion whereas uvula deviates towards opposite side.** For example:
 1. Right Hypoglossal nerve injury → tongue deviates towards right side + atrophy occurs.
 2. In Rt trigeminal injury → Jaw deviates towards right side (same side)
 3. Right Vagus injury → Uvula deviates toward left side
- **In CN XI (Spinal accessory nerve) injury**
 - i. weakness in turning head to contralateral side of lesion (Sternocleidomastoid muscle involved)
 - ii. Shoulder drooping on the side of lesion (Trapezius involved).
- In UMNL of facial nerve or Supranuclear palsy of facial nerve → contralateral lower facial (lower face) paralysis occurs + Forehead is spared. Because upper face (Forehead) receives contralateral supply from both sides.
- IN LMNL of facial nerve → ipsilateral upper + lower face paralysis – no sparing of Forehead

Uncrossed Hemiplegia	<ul style="list-style-type: none"> ○ Seen in Cortex/internal capsule/Supranuclear lesion, above the brain stem. ○ Ipsilateral limb paralysis + ipsilateral face involvement. For example: ○ Right sided facial muscle paralysis + Right sided limbs paralysis = Left Internal capsule lesion ○ Or the scenario may be like : Left sided deviation of mouth + Rt sided limb paralysis = Lt IC lesion ○ Because, left sided deviation is due to pull of healthy /normal left sided muscles towards their side. Hence, right sided facial paralysis and left sided deviation of mouth are both same things.
Crossed Hemiplegia	<ul style="list-style-type: none"> ○ Seen in brain stem lesion (pons/midbrain) Face and limbs/body opposite sides are involved. ○ For example: Right sided facial paralysis (palsy) + Left sided limb paralysis = Lesion in Pons

Posture:

- Extensor: Antigravity muscle (VIP make you stand up) → **Vestibulospinal tract** + Pontine Reticulo-spinal tract
- Flexor: Mnemonics = Sit on Rubber Mat → **Rubrospinal tract** and Medullary Reticulo-spinal tract

VENTRICULAR SYSTEM OF BRAIN

- There are 4 interconnected ventricles in the brain: 2 lateral ventricles, a third ventricle and a 4th Ventricle.

Lateral ventricles	<ul style="list-style-type: none"> • Largest of all ventricles, Bilateral C-shaped structures extending through all 4 brain lobes, they are separated by the septum pellucidum. • Each lateral ventricle has 4 parts: body or central part, anterior, posterior and inferior horn. • Each lateral ventricle communicates with the third ventricle via Foramen of Monro • It extends from interventricular foramen to septum pellucidum • Choroid plexus is present in inferior horn and body of lateral ventricle. <p><u>Boundaries of anterior horn:</u></p> <ul style="list-style-type: none"> • Anterior wall: Genu of corpus callosum • Roof of anterior horn is formed by Anterior part of body of corpus callosum • Floor formed by Rostrum of corpus callosum • Medial wall: septum pellucidum and lateral wall by head of caudate nucleus.
Third ventricle	<p>It is found in the midline within the diencephalon and communicate with the 4th Ventricle via Cerebral aqueduct which passes through midbrain.</p> <p><u>Boundaries:</u></p> <ul style="list-style-type: none"> ○ Anterior wall: anterior commissure, anterior column of fornix and lamina terminalis ○ Posterior wall: formed by posterior commissure, pineal gland and cerebral aqueduct. ○ Lateral wall Upper part: Medial surface of anterior 2/3rd of thalamus and smaller part is formed by hypothalamus, and it continues with floor of ventricle. ○ Floor is formed by optic chiasma, infundibulum, mammillary bodies, tegmentum of midbrain. ○ Roof formed by ependyma that stretches across upper limits of thalamus
Fourth ventricle	<ul style="list-style-type: none"> ○ Tent-like cavity of the hindbrain lined with ependyma and filled up with CSF. ○ it is situated in the posterior cranial fossa in front of the cerebellum and behind the pons and the upper part of medulla oblongata. ○ It's continuous inferiorly with the central canal of medulla oblongata and spinal cord, superiorly with the Cerebral aqueduct of the midbrain and dorsally has 1 median + 2 lateral apertures. ○ Median aperture/Foramen of Magendie: through it, fourth ventricle communicates with subarachnoid space. ○ Lateral apertures/Foramina of Luschka: for lateral communication with subarachnoid space. <p><u>BOUNDARIES</u></p> <ul style="list-style-type: none"> ○ Superolaterally is superior cerebellar peduncles and inferolaterally is inf cerebellar peduncle. ○ Roof or posterior wall is tent-shaped that projects into cerebellum. ○ Superior part of roof formed by superior medullary vellum + 2 sup cerebellar peduncles. ○ Inferior part of roof by inferior medullary vellum. ○ Roof is pierced in midline by foramen of magendie. ○ Floor/Rhomboid fossa: diamond- shaped, formed by posterior pons and upper medulla. ○ It is divided into left and right halves by median sulcus. ○ On each side of this sulcus there is an elevation called medial eminence in pontine part of floor at the level of facial colliculus.

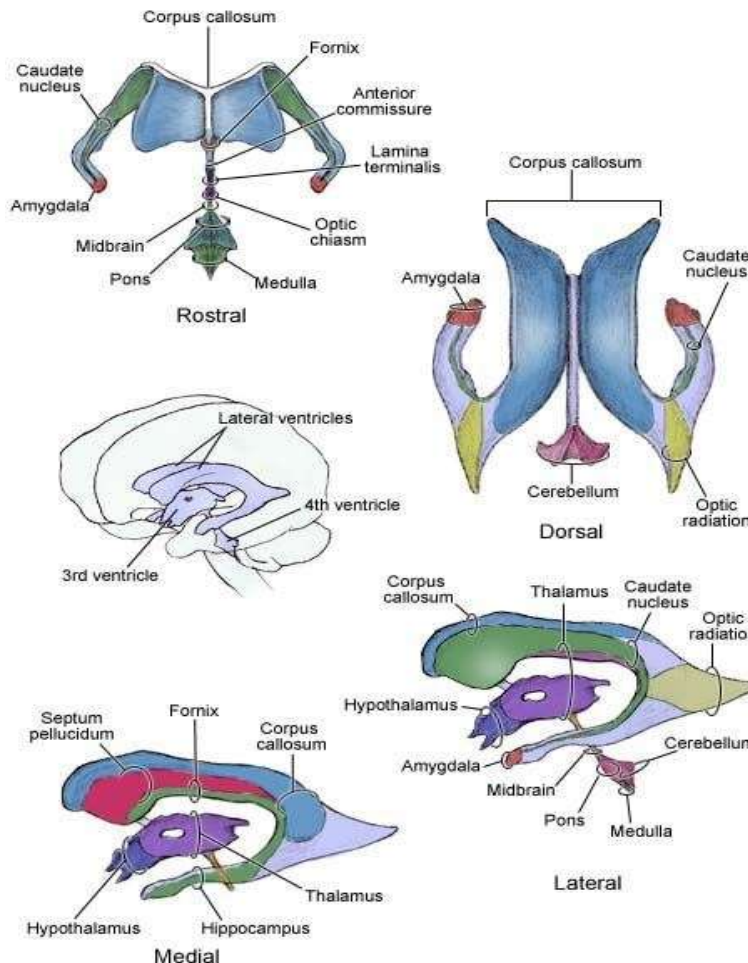
- On lateral of medial eminence is sulcus limitans, and lateral to sulcus limitans overlies vestibular nuclei.
- This sulcus divides the medial eminence in the medullary part of the floor into 2 Triangles: the hypoglossal triangle above and the vagal triangle below. These are inferior to stria Medullaris - glistening mass of white fibers derived from arcuate nuclei. Area postrema (BBB is absent here) is also present in floor b/w vagal triangle and lateral margin of ventricles.

Cerebral Aqueduct

- It is 1.8 cm, forms the cavity of midbrain, lined by ependyma, and, surrounded by Gray matter.
- Connects 3rd ventricle with 4th ventricle.
- Ascending reticular formation is present in the floor of the duct.
- The most common cause of congenital hydrocephalous is cerebral aqueduct stenosis

FLOW OF CSF

- Lateral ventricles → 3rd ventricle via right and left interventricular foramina of Monro
- 3rd ventricle → 4th ventricle via cerebral Aqueduct of Sylvius.
- 4th ventricle – subarachnoid space via Foramina of Luschka – lateral and Foramen of Magendie = medial.
- CSF made by choroid plexuses located in the lateral and fourth ventricles.
- CSF Travels to Subarachnoid space via foramina of Luschka and Magendie
- CSF is reabsorbed by arachnoid Granulations, and, then drains into Dural venous Sinuses.
- Choroid papilloma is mostly seen in lateral ventricle (children) and 4th ventricle (adults)



CEREBELLUM

- Situated behind pons & medulla, beneath the tentorium cerebelli in posterior cranial fossa.
- Weight is 150gm, consists of midline vermis + 2 lateral cerebellar hemispheres.
- The cerebellar cortex consists of multiple **parallel folds called folia** (leaf – like).
- **Anatomically** divided into three lobes:
Anterior, posterior (middle) and, the Flocculonodular (smallest and the oldest lobe).
- **Functionally** divided into 3 parts:
Archicerebellum (Vestibulocerebellum), Paleocerebellum (spino-cerebellum), and, Neocerebellum (neocerebellum is called the cerebro-cerebellum for programming and fine tuning of movements)
- **Morphologically** Cerebellum consists of 3 layers + 4 nuclei + 5 – 6 cell types as explained in table below.
- Cerebellum has largest population of inhibitory neurons in CNS.
- NO bipolar cells in cerebellum and only excitatory cells are **granule cells**.
- The granule cell synthesize glutamate but has GABA receptors. The Golgi cell inhibit granule cell via GABA receptors.
- Granule cells release Glutamate excite Purkinji cell.
- Basket and Satellite cell release GABA inhibit Purkinji cell
- Golgi cell release GABA inhibit Granule cells.
- **Purkinji cells release GABA inhibit Deep cerebellar nuclei.**
- Cerebellum modulates movement, central control of movement and aid in co-ordination and balance.
- Person stands against gravity due to cerebellum i.e maintenance of posture
- Vermis controls midline (axial) body parts.
- Limbs and facial regions in the intermediate zone.
- Large cerebellar hemispheres have no representation- role in planning and co-ordination of muscle movements.

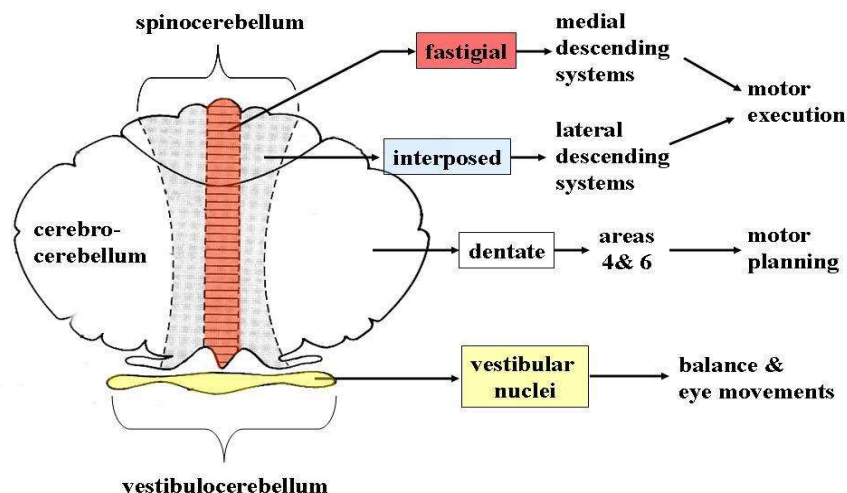
Layers & Cells		Nuclei	Input & Afferent	Output & Efferent
Outermost Molecular layer	Stellate cells Basket cells	Lateral to Medial (DEG – Fast) <ul style="list-style-type: none"> ▪ Dentate (largest) ▪ Emboliform ▪ Globose ▪ Fastigial (Medial most) Globose + emboliform = interposed nucleus	Input Travels via inferior + middle peduncles from cerebrum, pons, and spinal cord. Afferents: Mossy + climbing fibers Mossy fibers: from vestibular nucleus, pons, and spinal cord i.e vestibulocerebellar, pontocerebellar and spinocerebellar exert Excitatory terminals on granule cells. Climbing fibers: from inferior olivary nucleus, olivocerebellar exert excitatory on purkinji cells.	Travels via superior cerebellar peduncles from deep cerebellar nuclei. Purkinji cells are only output cells and always inhibitory.
Middle Purkinji layer	Purkinji cells (Only output) Inhibitory			
Inner Granular layer (deep)	3 Gs: Granule cells Golgi cells Glomeruli cells			

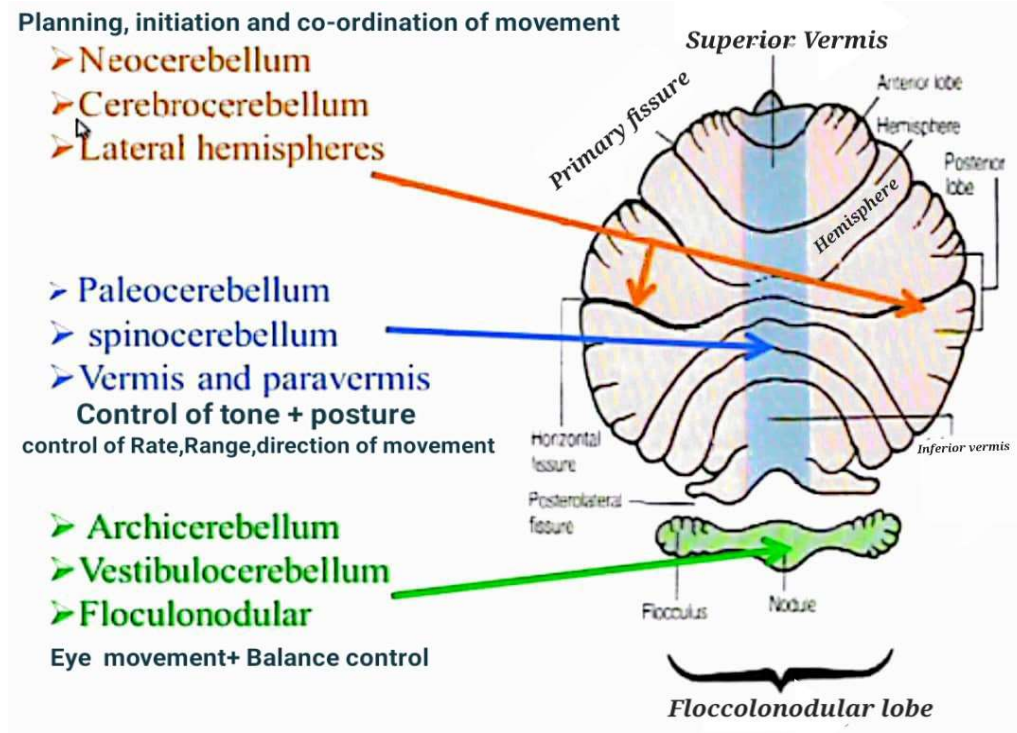
- Superior cerebellar peduncle (SCP): a paired structure of white matter that connects the **cerebellum to the midbrain**.
- Middle cerebellar peduncle (MCP): connect the **cerebellum to the Pons** and composed entirely of centripetal fibers.
Transverse fiber in pons makes middle cerebellar peduncle. MCP is the largest peduncle.
- Inferior cerebellar peduncle (ICP): a thick rope-like strand that occupies the upper part of the posterior **Medulla**.

Functions of Cerebellum	Lesions of Cerebellum	
<ol style="list-style-type: none"> Vermis/intermediate zone/ Spinocerebellum or Paleocerebellum: <ul style="list-style-type: none"> Synergy → control of rate, range, force, and direction of movement i.e ongoing motor execution Regulating tone and position of ongoing activity. Lateral hemisphere/Pontocerebellum or Cerebrocerebellum: Planning, initiation, and co-ordination of movement Via input from inferior olivary nucleus. Flocculonodular lobe/Vestibulocerebellum or Archicerebellum: Control of Balance and eye movement. Cerebellum controls fine movements and prevents overshoot of movement. Control of ballistic movements like Saccades and finger typing. 	Lesions of Vermis	<ul style="list-style-type: none"> Anterior Vermis: usually the result of degeneration from alcohol abuse and presents with gait ataxia Posterior Vermis: lesion result from medullo-blastoma and ependymomas, that present with truncal ataxia
	Lesion of hemispheres	<ul style="list-style-type: none"> Fall towards injured side (ipsilateral side) Dysmetria Dysdiadochokinesia – the characteristic sign Nystagmus (lesion of Flocculonodular) Intention tremors Scanning speech Hypotonia No muscle paralysis Fall with both open and closed eyes. Pendular Knee jerk Abnormal finger nose test Abnormal heel-knee shin test.

- Romberg's sign +ve = tendency to fall with eyes closed → sensory ataxia in DCML lesion
- If persons fall with either eyes open or closed → Cerebellar lesion
- Ataxia + Dysmetria are typical features of lesion in cerebellum.

Cerebellar Output





MEMORY						
Sensory or Immediate Memory (< 1 sec)	Short term or Working Memory (< 1 min)	Long term Memory (lifetime) (LTM)				
<ul style="list-style-type: none">For example, when you make a call on phone, you will remember that number only as long as you are calling soon after you forget it.Sensory memory gives decision time, prevents being overwhelmed, provides stability and recognition. <p>Types of Sensory Memory: Three types: iconic, eiconic, haptic</p> <ul style="list-style-type: none">Iconic: briefly stores an imageEconic: briefly stores a sound.Haptic: briefly stores a touch stimulus	<ul style="list-style-type: none">Lasts for 20 – 30 seconds, more information may be stored using chunking i.e break the information into 2 to 3 parts.Upto 7 to 8 chunks can be stored e.g Lo – Ili - pop.To remember a 7-digit phone numberAnd forgetting it sooner is an example of working memory. <p>Short term memory involves synaptic changes</p>	<p>Stores information for years. LTM formation involves structural changes and protein synthesis via gene activation. LTM has two types: Explicit and implicit.</p> <table><tr><td>Explicit memory</td><td>Also called declarative memory (conscious) Subtypes include: 1. Episodic memory: related to events or personal experiences or recollections. E.g remembering the date of birth/father name. 2. Semantic memory: Deals with facts + concepts. General Knowledge and info. related to the world. E.g earth is round, 2 +3 = 5.</td></tr><tr><td>Implicit memory</td><td>Also called procedural memory (Unconscious) E.g learning a skill, ride a bicycle and driving a car.</td></tr></table>	Explicit memory	Also called declarative memory (conscious) Subtypes include: 1. Episodic memory: related to events or personal experiences or recollections. E.g remembering the date of birth/father name. 2. Semantic memory: Deals with facts + concepts. General Knowledge and info. related to the world. E.g earth is round, 2 +3 = 5.	Implicit memory	Also called procedural memory (Unconscious) E.g learning a skill, ride a bicycle and driving a car.
Explicit memory	Also called declarative memory (conscious) Subtypes include: 1. Episodic memory: related to events or personal experiences or recollections. E.g remembering the date of birth/father name. 2. Semantic memory: Deals with facts + concepts. General Knowledge and info. related to the world. E.g earth is round, 2 +3 = 5.					
Implicit memory	Also called procedural memory (Unconscious) E.g learning a skill, ride a bicycle and driving a car.					

Upper Motor neuron lesion (UMNL)	<ol style="list-style-type: none"> 1. Increased Tone + reflexes (Exaggerated reflexes) 2. Babinski's sign +ve 3. Spastic paralysis + weakness 4. Clasp knife rigidity or spasticity 5. No atrophy/fasciculations 	Pseudo Bulbar palsy	<ul style="list-style-type: none"> o UMNL or Supranuclear lesion of: CN 9, 10, 12. o Gag reflex + jaw jerk: ↑/Normal o Dysarthria - Hot potato speech o Emotional liability present o Spastic Tongue, no fasciculation
Lower motor neurons lesion (LMNL)	<ol style="list-style-type: none"> 1. Decreased Tone + reflexes-hyporeflexia 2. Babinski's sign - ve 3. Flaccid paralysis + weakness 4. No clasp knife rigidity 5. atrophy/fasciculations present. 	Bulbar palsy	<ul style="list-style-type: none"> o LMNL or Infranuclear lesion of CN 9, 10, 12. o Gag reflex + jaw jerk: absent/↓ o Dysarthria – Nasal speech o No emotional liability o Wasted tongue + fasciculations

Part of brain	Important centres
Medulla	Respiratory, cardiac, vasomotor, vomiting, coughing, and swallowing.
Pons	Pneumotaxic center, Micturition (facilitatory center) , REM sleep center (locus cerulus of Pons)
Midbrain	Micturition inhibitory center. Prefer Pons for Micturition center.
Hypothalamus	Thirst and satiety , Temperature regulation (Pre-optic > Ant hypothalamus), vegetative functions
Temporal lobe	Olfaction, memory, taste, speech.

- **Frontal eye field lesion:** Eyes look towards the side of brain lesion (Opposite to hemiplegia)
- **Paramedian pontine reticular formation (PPRF) lesion:** Eyes look away from side of brain lesion
- **Medial longitudinal fasciculus lesion (MLF):** intranuclear ophthalmological i.e impaired adduction of ipsilateral eye, nystagmus of contralateral eye with abduction
- **Dorsal Midbrain lesion → Parinaud Syndrome:** vertical gaze palsy + convergence retraction nystagmus + Pupillary hyporeflexia (Pupillary light-near dissociation).

Neurotransmitter	Origin
Dopamine (Regulates emotions)	Substantia nigra pars compacta, Ventral tegmentum. Nigrostriatal pathway is rich in Dopamine Target of Dopa. are → striatum (basal ganglia) + frontal cortex.
Serotonin (Mood, hunger, sleep)	Raphe nucleus in brain stem (also center for slow wave sleep /NREM sleep) Target → cerebral cortex, striatum, Hippocampus, and cerebellum
Acetylcholine (For Memory)	Essential for Muscle action/learning. Source → Basal maynert nucleus, medial septum Target → cerebral cortex, amygdala, Hippocampus, thalamus, SNC, superior colliculus
Nor epinephrine or Nor-adrenaline	Required for mental alertness and arousal. Source → Locus cerulus Target → cortex, Hippocampus, and cerebellum

BLOOD SUPPLY OF CNS

SYSTEM	MAIN ARTERY	BRANCHES & SUPPLY
Vertebrobasilar (Posterior circulation)	1. Vertebral artery	<ul style="list-style-type: none"> ❖ Anterior spinal artery (ASA) : anterior 2/3rd of spinal cord + Medial medulla. ❖ Posterior inferior cerebellar artery (PICA): Lateral/ Dorsolateral medulla
	2. Basilar artery	<ul style="list-style-type: none"> ❖ Pontine arteries: supply base of pons ❖ Anterior inferior cerebellar artery (AICA) : inferior cerebellum + deep cerebellar nuclei ❖ Superior cerebellar: <ul style="list-style-type: none"> ❖ Labyrinthine (sometimes arises from AICA) : supplies inner ear
	3. Posterior cerebral artery	<ul style="list-style-type: none"> ❖ PCA supplies midbrain, thalamus, subthalamus, and occipital lobe. Also, the Inferior and lateral hemispheres (Occipital and posterior 2/3rd of the temporal lobe) ❖ Symptoms of occlusion: <ul style="list-style-type: none"> ➢ Contralateral hemianopia with macular sparing. ➢ Alexia without agraphia.

Internal Carotid (Anterior circulation)

1. Anterior cerebral artery:

- ❖ supplies Medial surface of hemispheres (Frontal, parietal, and upper temporal lobe), cingulate gyrus, internal capsule (anterior limb), ant corpus callosum, insula and operculum.
- ❖ primary motor cortex + sensory cortex especially **Leg/foot area**.
- ❖ Lesion results in contralateral spastic paralysis + sensory loss of **lower limb**, frontal lobe anomalies e.g urinary incontinence, transcortical apraxia of left limb (can understand command but cannot execute it).

2. Middle cerebral artery:

- ❖ Superolateral and lateral surface of hemispheres (including frontal, parietal and upper temporal lobe), internal capsule, basal ganglia, proximal visual radiations (Mayer loop)
- ❖ MCA gives Outer cortical and lenticulostriate branches.
- ❖ **Outer cortical branches:** supply the lateral convexity of hemispheres as mentioned before.
- ❖ **lenticulostriate branches:** main supply of the Internal capsule + Basal ganglia.
- ❖ **Lesion of MCA results in:**
 - **contralateral spastic paralysis and sensory loss of upper limb + face**
 - Aphasia due to Left MCA occlusion, left hemineglect due to Right MCA occlusion supplying the right parietal lobe.
 - contralateral superior quadrantanopia due to MCA supplying the Mayer Loop.

3. Anterior communicating artery: most common site of aneurysm.

4. Posterior communicating artery: 2nd common site of aneurysm, with CN III palsy in DM.

5. Ophthalmic artery: it gives Central retinal artery of retina, that is an end artery supplying retina and lesion may result in blindness.

IMPORTANT FACTS

Overall, Superolateral supply of hemispheres via MCA.
Medial surface by ACA and inferior + posterior surfaces by PCA.
Leg area supplied by ACA and Upper Limbs and Face are supplied by MCA.
Taste area, Speech areas, Auditory area, Superior temporal gyrus supplied via MCA
Brodmann area 4 or primary motor cortex supplied by ACA + MCA > MCA
Eye field is supplied by MCA, but visual field is supplied by PCA.
Primary motor area and internal capsule both supplied by ACA + MCA
Cingulate gyrus, paracentral lobule and Somesthetic cortex supplied by ACA.
Basal Ganglia insula, operculum, anterior temporal lobe and supplied by MCA
Ant communicating artery (A com) is ruptured mostly-- related to berry aneurysm
P Com is ruptured in Diabetes mellitus linked to Oculomotor/CN III palsy.
Posterior communicating artery passes over CN 3 to Connect to PCA to ICA.
Basilar artery to ICA is connected by P com
Pituitary gland is supplied by Hypophyseal arteries directly from ICA
Branches of vertebral artery: Meningeal, ASA, PICA, Basilar artery
Basilar artery gives AICA whereas Vertebral artery gives PICA (largest branch)
ASA is a branch of vertebral artery whereas Posterior spinal artery arises from PICA
Hence, Basilar artery gives AICA, Vertebral artery → ASA + PICA, PICA gives → PSA

CIRCLE OF WILLIS

- Anastomosis between anterior and posterior blood supplies to brain.
- Circle of Willis is formed by branches of 2 Internal carotid arteries + 2 vertebral arteries.
- It joins internal carotid arteries with Basilar artery. Basilar artery is formed by union of 2 vertebral arteries.
- Basilar artery terminates by giving 2 posterior cerebral arteries.
- Two ACA are joined by one Anterior communicating artery A com
- 2 Posterior communicating arteries P Com pass over CN 3 to Connect 2 PCA to 2 ICA
- 2 ACA + 1 A Com + 2 PCA + 2 P com takes part in formation of anastomotic network of circle of Willis.
- Major artery entering the brain and supplying it is ICA.
- Bleeding from ICA can be stopped by pressing at C6, also remember C6 – commencement of trachea + Esophagus
- Rupture of A Com is most commonly linked to Berry aneurysm rupture (in HTN or Polycystic kidneys patients).

BRAIN STEM SYNDROMES		
Medullary Syndromes	Medial Medullary syndrome	Lateral Medullary syndrome
	Anterior spinal artery (ASA) is involved. ❖ Ipsilateral spastic tongue paralysis with deviation of tongue on same side of lesion ❖ Tongue involvement* – key feature. ❖ Pyramids involvement leads to contralateral spastic paralysis. ❖ Medial lemniscus involvement: contralateral loss of touch, vibration, and proprioception.	Posterior inferior cerebellar artery is involved. (Wallenberg / PICA syndrome) ❖ Nucleus ambiguus: Dysphagia*, dysarthria , loss of gag reflex. These are characteristic features. ❖ Spinothalamic: Contralateral pain/temp loss-body ❖ Spinal trigeminal: ipsilateral pain/temp loss- face ❖ Inferior cerebellar peduncle: ipsilat. limb ataxia ❖ Vestibular nuclei: vertigo/vomiting/nystagmus ❖ Descending hypothalamus: ipsilateral Horner syndrome. ❖ No Face (motor) involvement in PICA syndrome
Pontine syndromes	Medial Pontine syndrome	Lateral Pontine syndrome
	Paramedian branches of basilar artery involved ❖ CN VI involvement: Medial strabismus* ❖ Corticospinal tract involved: leads to contralateral spastic paralysis. ❖ Medial lemniscus involvement: contralateral loss of touch, vibration, and proprioception ❖ As, the CN VI arises from Medial pons therefore features related to it are specific for Medial pontine syndrome	Anterior Inferior cerebellar artery is involved. AICA syndrome (or AICA Poop face) ○ Facial involvement: ipsilateral facial paralysis is the main feature as CN 7 arises from lateral Pons. Ipsilateral Loss of taste at anterior 2/3 rd of tongue+ lacrimation + salivation + hyperacusis ○ CN VIII fibers/Cochlear nucleus: Hearing loss on same side of lesion. ○ Vestibular nuclei: vertigo/vomiting/nystagmus ○ Middle cerebellar peduncle: Ipsilat limb ataxia ○ Spinothalamic: Contralateral pain/temp loss-body ○ Spinal trigeminal: ipsilateral pain/temp loss- face ○ Descending hypothalamus: ipsilateral Horner syndrome.
Midbrain syndromes	Medial Midbrain syndrome or Weber Syndrome • Branches of Posterior cerebral artery is involved. • Fibers of CN III: Ipsilateral oculomotor palsy → lateral strabismus + ptosis + dilated pupil • Corticobulbar tract: Contralateral hemiparesis of lower face • Corticospinal tract: Contralateral spastic paralysis	
Vertebrobasilar occlusion or Basilar artery thrombosis syndrome: Ipsilateral: ataxia, pain and temperature loss on face, Horner syndrome, loss of gag reflex, (dysphagia + hoarseness). Contralateral loss of pain and temp from body, hemianopia, vertigo, nausea/vomiting, cortical blindness, coma Locked in syndrome: → Quadriplegia + restricted eye movements.		
Concept Building to Easily diagnose the Brainstem syndromes		

Concept Building to Easily diagnose the Brainstem syndromes

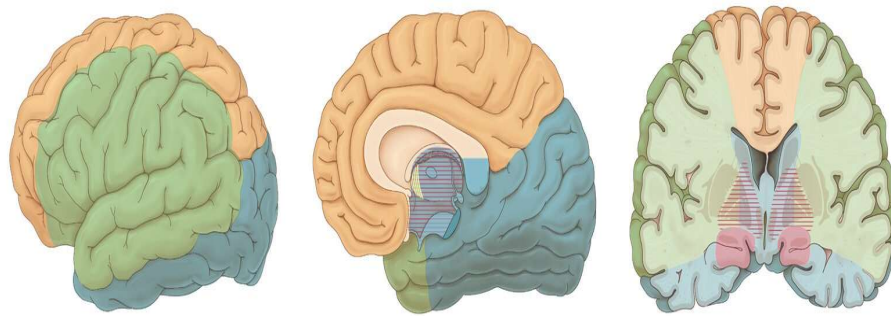
There is lot of confusion, misunderstanding and phobia related to brain stem syndromes in Students. Reading the conceptual points given below will help in diagnosing the scenarios.

- Corticospinal tract + Medial lemniscus involved in both Medial syndromes i.e., medullary & Medial pontine.
- Spinothalamic + spinal trigeminal + cerebellar + vestibular + descending hypothalamus are involved in both Lateral syndromes i.e lateral medullary + lateral pontine syndromes. So, their symptoms are same in both.
- ASA supplies Medial medulla. **Tongue involvement** is seen in medial medullary syndrome due to Hypoglossal nerve arising from midline/center of medulla. So, where in scenario you find Tongue paralysis go with → ASA.
- PICA supplies lateral medulla, contains nucleus ambiguus → lesion causes ipsilateral paralysis of muscles of pharynx, larynx etc. **Dysphagia** is the important feature of PICA syndrome.
- Medial pons supplied by paramedian pontine branches of Basilar artery, contains CN 6 nucleus. The features related to Abducent nerve will be present in Medial pontine syndrome i.e **Medial squint/Convergent strabismus**.
- Lateral pons is supplied by AICA and has CN 7 nucleus. Involvement of AICA will lead to symptoms related to CN 7 i.e ipsilateral loss of taste at ant 2/3rd tongue + loss of salivation, lacrimation, corneal reflex and hyperacusis.

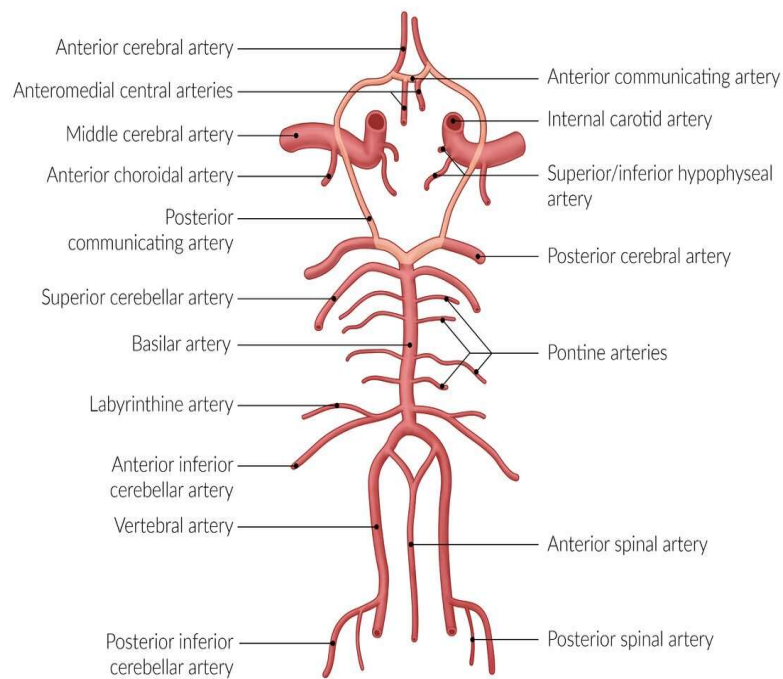
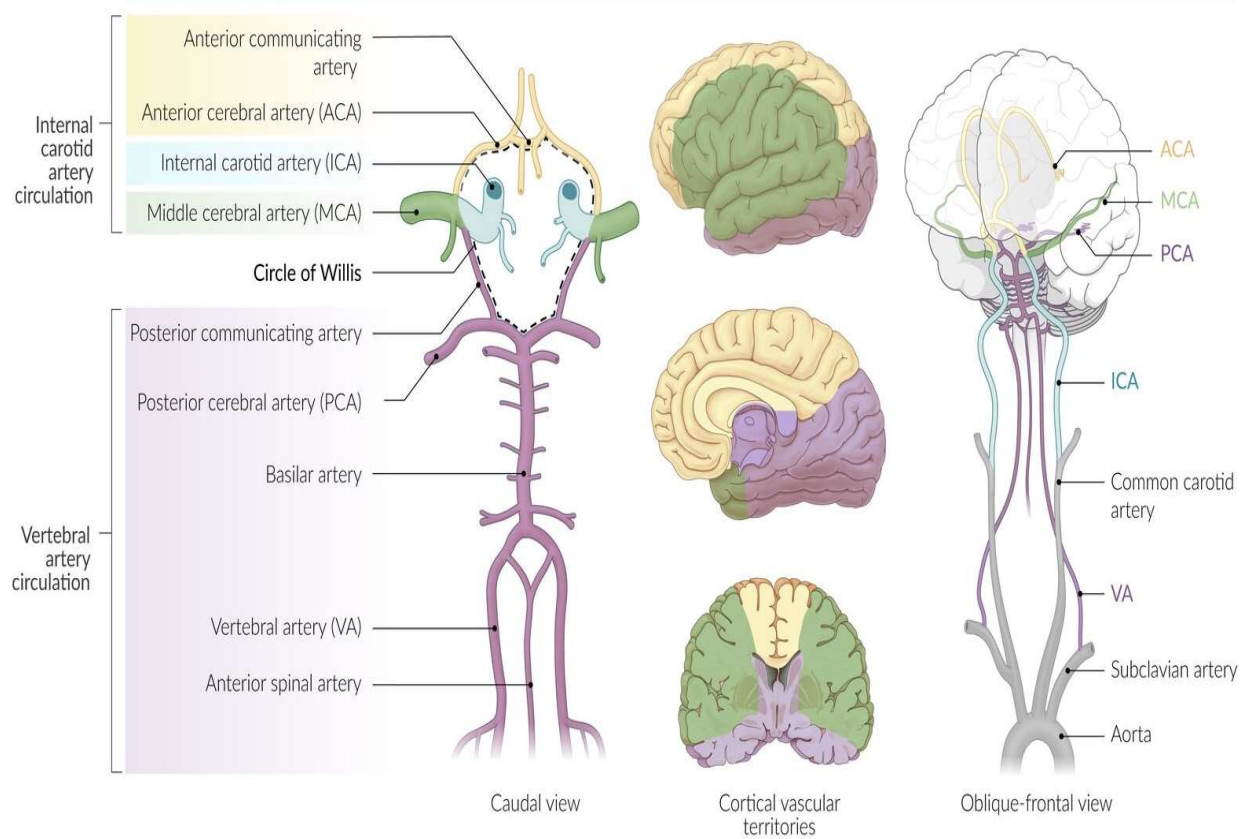
As AICA syndrome has **typical Facial involvement**, hence, it is called AICA Poop face/drooped face.

- Medial Midbrain has CN III nuclei, so the features related to ipsilateral **oculomotor palsy** alongwith contralateral hemiplegia are present.
- **Locked in syndrome** seen in Basilar artery thrombosis (Quadriplegia, restricted eye movements and Coma)

1. Permanent Coma	➤ Thalamus involved
2. Deep Coma	➤ Locus cerulus involved
3. Prolonged coma	➤ Periaqueductal gray matter involvement



- Anterior cerebral artery
- Middle cerebral artery
- Partially supplied by posterior communicating artery
- Posterior cerebral artery
- Anterior choroidal artery
- Partially supplied by anterior choroidal artery



STROKE

ISCHEMIC STROKE (85%)

- Due to Occlusion of vessel by thrombus/embolus.
- Thrombus is more common than embolism
- Most common vessel involved is MCA
- Irreversible neuronal injury occurs after 5 min of hypoxia.
- Pyramidal cells of Hippocampus and Purkinji cells of cerebellum are most vulnerable to ischemia in brain.
- Thyrotoxicosis can lead to A Fib and embolic stroke.
- Mitral stenosis is also linked to ischemic stroke.

HEMORRHAGIC STROKE (15%)

- Due to rupture of vessel by trauma, fragile vessel in aging process or congenital malformations.
- it includes intraparenchymal hemorrhage (8%), epidural + subdural hematoma and subarachnoid hemorrhage
- There is a risk of conversion of Ischemia into hemorrhage in acute stroke. Therefore, some clinicians delay the thrombolysis till 2 – 3 days.
- Thrombolysis is contraindicated

Symptoms common to All kinds of stroke are: (Mnemonics BE – FAST)

- **B** – Balance loss (sudden loss of balance and co-ordination, Headache, dizziness)
- **E** – Eyesight changes (Blurred or double vision)
- **F** – Facial drooping (facial asymmetry)
- **A** – Arm weakness (or leg weakness on one side of body)
- **S** – Speech difficulty (e.g Slurred speech, unable to speak or difficult to understand)
- **T** – Time to call for help (Call 1122 – in Pak, 911 - USA/Canada, 999 – UK and 000 – Australia)

CT scan without contrast is the investigation of choice in acute stroke. MRI is less sensitive in acute stroke (48hrs).

CT Brain Findings in ischemia:

Hypodense areas due to loss of blood flow and tissue death + loss of gray-white matter differentiation.

Initially it is difficult to diagnose ischemia even by CT.

However, CT is helpful for initial investigation.

Later, MRI and other blood tests including Lipid profile are required.

CT Brain findings in hemorrhage:

Hyperdense areas (brighter regions) due to blood accumulation at that area.

Intraparenchymal hemorrhage appear as irregularly

we can say that hemorrhagic appears as dark Black areas

(Hyperdense) on CT brain and ischemia presents as white areas

(Hypodense) on CT

TYPES OF ISCHEMIC STROKE & MANAGEMENT

1. **Thrombotic** – clot formation directly at the site of infarction over ruptured atherosclerotic plaque (most commonly MCA)
2. **Embolic** – embolism from other site body lodges in vessel (e.g MCA) in atrial fibrillation
3. **Hypoxic** – due to hypoperfusion or hypoxemia e.g in cardiac surgery and tends to affect watershed areas.

Management

- Blood glucose, temperature, hydration and O2 saturation to be maintained alongwith nursing care.
- Exclude the hemorrhage by Non-contrast CT
- Thrombolysis (**tPA**) is the mainstay of treatment within 3 – 4.5 hours (ideally within 2 hrs).
- Current NICE guidelines suggest the use of **Alteplase**
- Thrombectomy/embolectomy in large vessel occlusion
- with regards to A fibrillation, Anticoagulants shouldn't be started until Imaging has excluded hemorrhage and usually not until 14 days have passed after ischemic stroke due to risk of hemorrhagic transformation.
- Optimum control of blood pressure – do not lower BP in acute stroke unless complications like hypertensive encephalopathy.
- Smoking cessation, statins if cholesterol > 3.5mmol/l
- Treat the underlying cause e.g atrial fib/ carotid artery stenosis

Contraindications to Thrombolysis**TYPES OF HEMORRHAGE AND MANAGEMENT****Epidural hematoma (EDH)**

- Due to rupture of anterior div of middle meningeal artery 2ndry to RTA/ Skull fracture.

- **Lucid interval** present – pt. Is conscious for some time after which becomes unconscious.

★**CT brain** shows Lentiform, or lens shaped biconvex hyper dense hemorrhage **Not** crossing the suture lines.

Management → Craniotomy
Or Burr hole craniotomy

Subdural hematoma (SDH)

Trauma or brain atrophy in old age leads to rupture of bridging veins / Superior cerebral vein

May be acute, subacute/, chronic.

Acute – Hyperdense on CT

Chronic – Hypodense on CT

On CT: Crescent shaped, **crossing** midline.

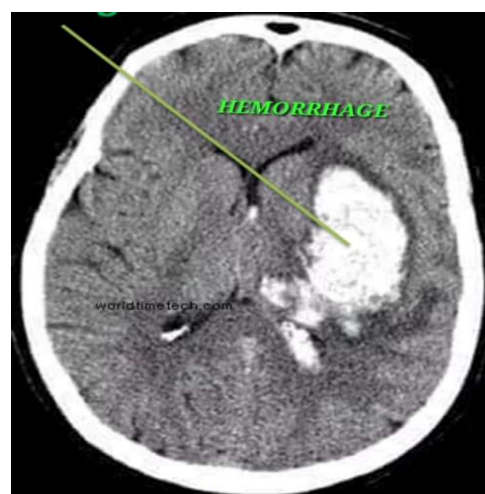
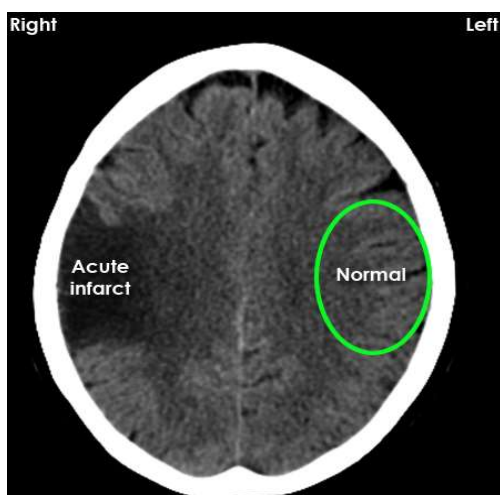
Managed by Craniotomy.

Subarachnoid hemorrhage (SAH)

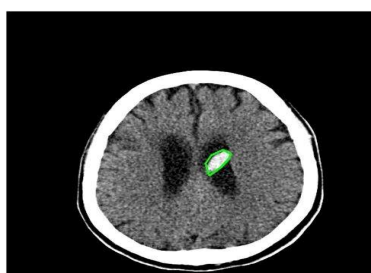
Bleeding due to RTA or rupture of aneurysm (Berry) leads to: ■ Worst headache of one's life

- Neck stiffness (meningism)
- Risk of hydrocephalus is inc.
- CT angiogram for diagnosing
- Xanthochromic CSF on exam.

Absolute	acute hemorrhage, previous intracranial hemorrhage, active bleeding, stroke or head injury in past 03 months, GI bleed in past 03 weeks, pregnancy, Uncontrolled HTN, Intracranial neoplasm, seizure at stroke onset subarachnoid hemorrhage.	<ul style="list-style-type: none"> Nimodipine reduces the risk of vasospasm, as there is risk of re-bleed in 3 – 10 days. Clipping or coiling can be done.
Relative	Major surgery or trauma in preceding 02 weeks, intracardiac thrombus, hemorrhagic diathesis – INR > 1.7, hemorrhagic retinopathy in DM	<p>Intraparenchymal hemorrhage</p> <p>Most commonly seen in HTN i.e Charcot-Bouchard microaneurysm In lenticulo-striate vessels that supply Basal ganglia, especially Lentiform nucleus is involved followed by thalamus, pons, and cerebellum. Reperfusion injury in ischemic stroke may also be the cause</p>



(a) IPH



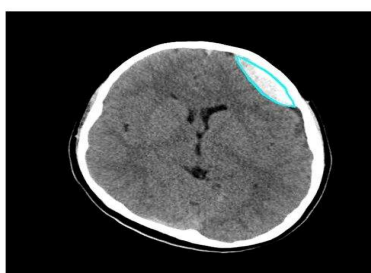
(b) IVH



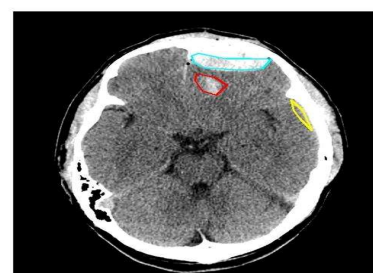
(c) SAH





(d) SDH



(e) EDH



(f) Multiple

TRANSIENT ISCHEMIC ATTACKS	NEONATAL INTRAVENTRICULAR HEMORRHAGE
<ul style="list-style-type: none"> Brief, reversible episode of focal neurological dysfunction without acute infarction, MRI brain – no findings. TIA resolves in < 15 minutes and should not last more than 24 Hrs. They don't cause any permanent damage to brain But they forecast or are precursor of cerebrovascular event. May present with amaurosis fugax – transient vision loss due to retinal artery emboli. TIA's don't require any treatment. 	<ul style="list-style-type: none"> Seen in premature or low birth weight infants due to reduced glial fiber support + impaired autoregulation of B.P, leads to bleeding in germinal matrix of subventricular zone that is highly vascularized. USG shows blood in intraventricular spaces May present with altered level of consciousness, seizure, bulging fontanelle, hypotension, and coma.
WATERSHED ZONES	
<ul style="list-style-type: none"> Cortical border zones occur between ACA – MCA and PCA – MCA Internal border zones occur between the Superficial and deep vascular territories of MCA 	<ul style="list-style-type: none"> Common locations for brain metastases. Infarct due to severe hypoperfusion: <ul style="list-style-type: none">  ACA-MCA watershed infarct → proximal Upper and lower extremity weakness (man- In-a-barrel syndrome).  PCA- MCA watershed infarct → higher-order Visual dysfunction.

HEADACHES	
(Pain due to irritation of structures such as dura, cranial nerves, or extra cranial structures)	
Primary headaches	Migraine, Tension, and cluster headache. Migraine and tension headache are more common in Females > Males.
Secondary headaches	Meningitis, subarachnoid hemorrhage, TMJ, Hypertension, neoplasia, hydrocephalus, giant cell arteritis and sinus headache etc.
PRIMARY HEADACHES	
MIGRAINE	<p>Unilateral pulsating headache with nausea, vomiting, photophobia, phonophobia and ± aura.</p> <p>Aura is a perceptual disturbance, manifests as the perception of a strange light, unpleasant smell, or confusing thoughts/experiences. Diagnosis with aura is easy.</p> <p>Pain is due to irritation of CN V, meninges, or blood vessels → release of vasoactive neuropeptides e.g substance P or calcitonin gene related peptide</p> <p>Headaches may last for 4 – 72 hours even.</p> <p>Treatment: For acute attacks → Oral Sumatriptan – 5HT₁ agonist (serotonin agonist) is the drug of choice. Zolmitriptan can also be used. Give Oral Triptans + NSAID or Oral triptans + paracetamol.</p> <p>2nd line: IV Metoclopramide or Prochlorperazine + (IV/IM NSAID or Triptan)</p> <p>Migraine in Pregnancy: 1st line is paracetamol 1gm. 2nd line – Aspirin 300mg or Ibuprofen 400mg in first or second trimester.</p> <p>Migraine and OCP: if patient have migraine with aura. Combined OCPs - absolutely contraindicated.</p> <p>Migraine and HRT: HRT can be given with migraine history, but it can worsen migraine sometimes.</p> <p>Prophylaxis: Pizotifen is no longer recommended now.</p> <p>1st line – Propranolol or Topiramate. Other options: Amlodipine, SSRIs/TCA</p> <p>2nd line – Gabapentin or Riboflavin (Vit B2)</p> <p>Pregnancy: Propranolol is preferred as Topiramate is teratogenic agent.</p> <p>Predictable menstrual migraine: Zolmitriptan 2.5 mg 1 × B.D / T.D.S per day.</p>
Tension Headache	<p>Bilateral Band like steady pain constant for > 30 minutes (4-6 hrs typically) without photophobia, phonophobia or aura. Treated with NSAIDS, Acetaminophen.</p> <p>For prophylaxis use TCAs (Amitriptyline). Behavioral therapy can be done.</p>
Cluster Headache	<p>Unilateral excruciating periorbital pain (suicide headache) + autonomic features i.e lacrimation, runny nose and conjunctival redness.</p> <p>May last for 15 min – 3hr, repetitive and more common in males.</p> <p>May present with Horner syndrome.</p> <p>Acute cases: Sumatriptan, 100 % O2. For prophylaxis use Verapamil</p>

TRIGEMINAL NEURALGIA

Unilateral repetitive **shooting/shock like pain** in the trigeminal nerve distribution that is triggered by chewing, talking or touching certain areas on face. Lasts for seconds to minutes.
but episodes increase in frequency and intensity over time. First line drug is **carbamazepine**

NEUROLEPTIC MALIGNANT SYNDROME	IDIOPATHIC INTRACRANIAL HYPERTENSION
<p>A rare but dangerous complication of typical antipsychotic drugs (e.g., Haloperidol, chlorpromazine, thioridazine) caused by sudden reduction in dopamine activity either from Dopamine receptor blockade or withdrawal of dopaminergic agents.</p> <p>Presents with Fever, muscle rigidity, myoglobinuria, hemodynamically instability and encephalopathy even.</p> <p>Treatment protocol includes reducing the Body temp. with antipyretics, IV hydration to prevent renal failure. Dantrolene and D2 agonists e.g Bromocriptine.</p>	<p>Raised Intracranial pressure without any apparent cause like hydrocephalus on CT/MRI.</p> <p>More common in Obese females, may be linked to Vit A excess, tetracycline or danazol.</p> <p>Presents with headache, diplopia, papilledema, normal mental status.</p> <p>LP reveals increased Opening pressure > 20cm H₂O and it relieves the headache as well.</p>

HERPES SIMPLEX ENCEPHALITIS

- Caused by HSV – 1, typically **affects temporal lobe > Inferior frontal lobe**. Presents with fever, headache, aphasia, seizures, vomiting, psychiatric features, and focal neurological deficits
- **PCR for HSV – 1 is diagnostic in 90% cases.**
- CT shows petechial hemorrhages in temporal lobe mostly and frontal lobe.
- MRI is preferred than CT here as CT is normal in 1/3rd of cases.
- EEG shows low frequency (2 Hz) lateralized periodic discharges.
- It can be treated with IV Acyclovir and prognosis depends upon early start of acyclovir therapy.
- In untreated cases, mortality approaches 80 – 85%.

HEAD INJURY & TRAUMATIC BRAIN INJURY (TBI)**Classification According to:**

Type of injury	<p>Open, closed, blunt and penetrating.</p> <p>Blunt injury/non-missile injuries: Moving head strikes a fixed Object or a moving object strikes an immobile head leads to scalp injury, Fractures of the skull and contusions of Brain</p> <p>Injuries resulting from rapid Deceleration of the head causing the brain to move within the Cranial cavity and to encounter bony protuberances Within the skull.</p> <p>Penetrating Injuries may be high velocity (bullet injury) or low velocity. High velocity injury causes death due to impaction of medulla and cerebellum into foramen magnum.</p>
Site of injury	<p>Scalp injury: laceration and subgaleal hematoma (it develops b/w skull periosteum and scalp aponeurosis and crosses suture lines, common in neonates – associated with forceps delivery)</p> <p>Skull injury: Open fracture (has risk of intracranial hematoma) or closed fracture – has risk of serious infection, cover it with a sterile dressing that has been moistened with sterile saline.</p> <p>Depressed skull fracture, liner fracture or Basilar (Base of skull) fracture.</p> <p>Basilar fracture is associated with Raccoon eyed/panda eyes (periorbital ecchymosis), Battle sign – bruising over mastoid, bleeding from nose/ears and CSF leakage/rhinorrhea (it is a clear fluid vs nasal secretion that are sticky and a little thicker, beta 2 transferrin is diagnostic for CSF rhinorrhea).</p> <p>BRAIN INJURY: may be primary (immediately) or secondary (minutes to days).</p> <div style="background-color: #e6f2ff; padding: 5px;"> <p>Primary Brain injuries: cerebral concussion, contusion, laceration, and diffuse axonal injury</p> <ul style="list-style-type: none"> • Cerebral concussion is slight distortion causing temporary physiological changes leading to transient loss of consciousness with complete recovery. • Cerebral contusion is more severe degree of damage with bruising and cerebral oedema leading to diffuse or localized changes. • Cerebral laceration is tearing of brain surface with collection of blood in different spaces and with displacement of dural parts. </div>

	<ul style="list-style-type: none"> Diffuse axonal injury – This type of brain damage occurs as a result of mechanical shearing following deceleration, causing disruption, and tearing of axons at the grey/white matter interfaces <p>Secondary brain injuries: cerebral Edema, infection, cerebral ischemia, Epilepsy, and hematoma.</p> <p>Intracranial vascular injury: EDH, SDH, SAH, intracerebral hemorrhage</p>		
Severity of injury	<p>Mild</p> <ul style="list-style-type: none"> GCS 13 – 15 No loss of consciousness (LOC) Amnesia < 30 min. 	<p>Moderate</p> <ul style="list-style-type: none"> GCS 9 – 12 LOC: 30 min – 24 hrs Amnesia: 1 – 7 days 	<p>Severe</p> <ul style="list-style-type: none"> GCS 3 – 8 LOC: > 24 hours Amnesia: > 7 days
Pathology of injury	<p>Effects of Brain Injury</p> <ul style="list-style-type: none"> Brain oedema is accumulation of fluid, both intracellular and extracellular, it is due to congestion and dilatation of blood vessels. It may be diffuse or localized. Brain necrosis is of severe variety with destruction and is due to haemorrhagic infarction. Brain ischemia is due to increased pressure leads to alteration in the perfusion of brain which itself aggravates the ischaemia and this forms a vicious cycle, causing diffuse ischaemia of brain. Coup injury occurs on the side of the blow to the head. Contre-coup injury occurs on the side opposite to the blow on the head. Coning: it is due to ↑ ICP causing either herniation of supra-tentorial or infra-tentorial contents. Supratentorial herniation: through tentorial hiatus causing compression ipsilateral CN III and Midbrain Infratentorial herniation: through foramen magnum that compresses the cerebral aqueduct. 		
Clinical features of TBI	<p>Headache, Projectile Vomiting, amnesia, loss of consciousness or altered orientation and mental status, Pupil changes, body temperature changes, disturbed vision, poor sleep and speech, loss of balance and focal neurological deficits e.g Limb weakness.</p> <p>Cushing Reflex: Bradycardia +Hypertension +Irregular respiration /Cheyne stoke's breathing</p>		
Complications of TBI	<p>Brainstem injury due to coning, cerebral edema, Loss of memory, post-traumatic headache, epilepsy, meningitis, hydrocephalus, CSF rhinorrhea/ leakage, Cushing's ulcers, SIADH, low Na hyperthermia, arrhythmias, bleeding, shock, acute kidney and lung injury, coma and death.</p>		

Clinical Assessment

Primary survey: includes Airway, Breathing, circulation, disability, and exposure (ABCDE)

Neurological Assessment: for Loss of consciousness, GCS scale, pupils' reaction to light and size, Vitals, reflexes, and limb movements.

Secondary Survey: look for any fractures (skull/pelvic), abomino-thoracic injuries, skull hematomas and CSF leakage from ears or nose.

Management of TBI & Raised Intracranial Pressure

- Head elevation → Prop up 30° - 45° and Straighten neck – avoid any neck tape that encircles it.
- Respiratory support: intubation or ventilation
- Avoid hypotension (SBP < 90 mmHg) and control hypertension, also Avoid hypoxia (PaCo₂ < 60 mmHg)
- Control ventilation (aim: PaCo₂ 30 – 45 mmHg) and Adequate sedation (barbiturates) + muscle relaxants.
- Diuretics (Mannitol 1g/kg or Inj Lasix 40mg), seizures control (Inj Lerace 500mg IV)
- Temperature and vomiting control by Inj Falgan 1gm IV + Inj Gravinate IM /Inj Onset IV.
- Do CT brain and hospitalize according to criteria of NICE guidelines.
- Surgical management** includes evacuation of focal hematomas EDH/SDH via Burr hole/ craniotomy, CSF drainage via ventriculostomy, delayed evacuation of hematoma and decompressive craniotomy.

INDICATIONS OF CT BRAIN					
Immediately			Within 08 hrs		
<ul style="list-style-type: none">GCS < 13 on initial assessmentGCS = 13 or 14 at 2 hours post-injurySuspected open or depressed skull fracture.Any sign of basal skull fracture (hemotympanum, 'panda' eyes, Battle's sign, CSF fluid leakage from the ear or nose).Post-traumatic seizure.Focal neurological deficit.More than 1 episode of vomiting			<p>For adults with any of the following risk factors who have experienced some loss of Consciousness or amnesia since the injury:</p> <ul style="list-style-type: none">Age 65 years or olderAny history of bleeding or clotting disordersIf a patient is on warfarin who has sustained a head injury with no other IndicationsDangerous mechanism of injury: Pedestrian or cyclist struck by a motor vehicle, An occupant ejected from a motor vehicle or fall from a height of greater than 1 metre or 5 stairs30 minutes' retrograde amnesia of events immediately before the head injury		

GLASSGOW COMA SCALE (3 – 15)

- To assess the severity of head injury and describe the level of consciousness in TBI.
- It has 3 components: Eye (E) , Verbal (V) and Motor (M) → EVM
- Maximum score is 15 and minimum is 3 , as no response carries 1 score for each.

Eye Opening		Verbal response		Best motor response	
Spontaneous	4	Oriented	5	Obeys command	6
To Loud noise	3	Confused	4	Localized pain	5
To pain	2	Inappropriate words	3	Withdraws (flexion)	4
No response	1	Incomprehensible Sounds	2	Abnormal flexion posturing	3
		None	1	Extension posturing	2
				None	1

Cerebral Perfusion & Cerebral Perfusion Pressure

<ul style="list-style-type: none">Relies on tight autoregulation.Primarily driven by Pco2.Po2 also modulates perfusion in severe hypoxiaCerebral Perfusion also depends on a pressure gradient between (MAP) and (ICP)↓ BP ↑ ICP → ↓ cerebral perfusion pressure (CPP)Cushing reflex: triad of hypertension, Bradycardia, and respiratory depression in Response to raised ICP	<h4>Therapeutic hyperventilation</h4> <p>↓ Pco2 → Vasoconstriction → ↓ cerebral blood flow → ↓ ICP. May be used to treat acute cerebral Edema (e.g in stroke) unresponsive to other Interventions.</p> <p>CPP = MAP – ICP. If CPP = 0, there is no Cerebral perfusion → brain death</p> <p>Hypoxemia increases CPP only if Po2 < 50 mmHg.</p> <p>CPP is directly proportional to Pco2, until Pco2 > 90 mmHg</p>
--	--

SEIZURES & EPILEPSY						
SEIZURES	Synchronized, paroxysmal and abnormal high frequency neuronal firing or discharge in CNS.					
	Causes of seizures by Age					
	Children → genetic, infection (febrile fits), trauma, congenital and metabolic (hypoxia) causes.					
	Adults → trauma, tumor, stroke, and infections play role.					
	Elderly → stroke, tumor, trauma, metabolic (hypoglycaemia, hypocalcaemia, hypoNa+), infection.					
Variety of seizures exist as follows:						
Partial or Focal seizures	Affect single area of brain, most commonly originate in the medial Temporal lobe. Partial or focal seizures may be Simple or complex.					
	Simple partial	Begin as jerking on one side of mouth or hand. May be motor, sensory, autonomic, and psychic. No loss of consciousness and no post-ictal confusion. Examples: <table><tr><td>Jacksonian seizures</td><td>Todd's palsy</td></tr><tr><td>Also called focal/partial motor seizure that begin as jerks on one side of mouth/hand and may spread to involve entire side.</td><td>Paralysis of involved limb after a seizure with complete recovery in 24 hours.</td></tr></table>	Jacksonian seizures	Todd's palsy	Also called focal/partial motor seizure that begin as jerks on one side of mouth/hand and may spread to involve entire side.	Paralysis of involved limb after a seizure with complete recovery in 24 hours.
	Jacksonian seizures	Todd's palsy				
Also called focal/partial motor seizure that begin as jerks on one side of mouth/hand and may spread to involve entire side.	Paralysis of involved limb after a seizure with complete recovery in 24 hours.					
Complex partial	Impaired consciousness + automatism present with post- ictal confusion. It begins as repetitive blinking of eye or lip smacking, and they can't interact with people normally. Example given as: Temporal lobe epilepsy presents with sensation of <i>deja vu</i> (undue familiarity), <i>Jamais vu</i> (unreal feeling) and may progress to hallucinations and altered consciousness.					
Generalized Seizures	They are diffuse and simultaneously arise from bilateral cerebral hemispheres. Types → Tonic-clonic, absence, myoclonic, tonic, and atonic.					
	Tonic – clonic seizures	Also known as Grand- mal epilepsy, present with alternating stiffness and movement with loss of consciousness + tongue-biting + urinary incontinence and post-ictal confusion				
	Absence seizures or Petit-mal epilepsy	Short and frequent episodes of blank stares, no post-ictal confusion and the person seems to be day dreaming. Mostly seen in female child. 3 Hz spike and wave electric discharge on EEG brain. Prefer, spike and wave (slow wave) > spike and dome.				
	Myoclonic	Quick and repetitive jerks.				
	Tonic	Stiffening episodes				
	Atonic	Drop seizures -- falls to floor, mistaken for fainting.				
EPILEPSY	Disorder of recurrent, unprovoked seizures due to chronic underlying process (except fever)					
STATUS EPILEPTICUS	Continuous seizures (> 5 – 30 min) or recurrent seizures without regaining awareness between attacks that may result in brain injury. May be idiopathic or initial presentation of epilepsy, due to sleep deprivation in epileptic patient, severe hypoxic encephalopathy and any current illness going on. Sudden withdrawal of anti-epileptic drugs is the most common cause. Management: it is a serious medical emergency. <ul style="list-style-type: none">• Maintain Airway, breathing and circulation, Give O2 8-10 L/min, IV access -- give fluids (NS).• Keep the patient in semi-prone position to avoid the risk of aspiration.• Draw samples for Blood CBC, glucose, calcium, and Urine toxicology screen.• Administer IV/rectal Lorazepam, if pt. Doesn't respond repeat after 5-10 minutes.• If seizures recur/fail to respond after 30 min, give IV Phenytoin/Fosphophenytoin 18mg/kg.					

- If still seizures persist, induction of general anaesthesia with propofol or thiopental + assisted ventilation and once seizures are controlled → give long-term anticonvulsant therapy with Sodium valproate or phenytoin and investigate the underlying cause.

TREATMENT OF SEIZURES & EPILEPSY

- **Partial seizures:** 1st line treatment: Carbamazepine (phenobarbital in neonates), others are lamotrigine and sodium valproate. Carbamazepine blocks Na⁺ channels and may cause ataxia, teratogenic (cleft palate, Spina bifida)
- **Tonic – clonic:** Sodium valproate is DOC. Lamotrigine is alternate drug. Na – valproate blocks Na⁺ channel + ↑ GABA.
- **Absence seizure:** Ethosuximide is DOC. Alternate is Na-valproate, avoid carbamazepine (may exacerbate)
- Ethosuximide blocks T-type calcium channels in neurons. Side effect is GIT distress.
- **Myoclonic:** Sodium valproate is 1st line drug. Clonazepam is alternative.
- **Status epilepticus:** Benzodiazepines (diazepam), phenobarbital, phenytoin. Prefer benzodiazepines.
- **Epilepsy in pregnancy:** pregnant females should receive 5mg folic acid to avoid neural tube defects. **Carbamazepine** is preferred. Lamotrigine dose needs to be increased.
- **Valproic acid/Na – valproate** may cause Spina bifida and craniofacial anomalies. Severely hepatotoxic.
- **Phenytoin:** is teratogenic (cleft palate), others S/E: bleeding, hirsutism, coarse facial features, gingival hyperplasia.
- **Breast feeding:** it is safe with treatment, except barbiturates.
- Phenytoin + carbamazepine → Cytochrome P - 450 enzyme inducers, Valproic acid → Cyt- P 450 inhibitor.

NEURODEGENERATIVE DISORDERS

- They result in cognitive ability, memory or function with intact consciousness.
- They include, Parkinson disease, Huntington's disease, Alzheimer disease and various dementias.
- Psuedodementia may occur in depression, other reversible causes of dementia are hypothyroidism, B12 deficiency, neurosyphilis and normal pressure hydrocephalus.

Parkinson disease	<ul style="list-style-type: none"> ○ Loss of dopaminergic neurons of substantia nigra pars compacta → ↓ Dopamine. ○ Characterized by Lewy bodies (intracytoplasmic eosinophilic inclusions) composed of alpha in damaged neurons. ○ Causes: Most common—idiopathic, others are trauma, drugs, and toxins (Methylphenyltetrahydro-pyridine – toxic to substantia nigra) ○ Clinical features: RAFTS: Rigidity, Akinesia, Flat facies, Tremors (pill rolling), Shuffling gait. ○ Dementia is a late finding. Akinesia/bradykinesia may occur. Rigidity – Cogwheel type. ○ Disease presents mostly after 50-60 yrs of age. <p>Shy-dragger syndrome = parkinsonism + autonomic dysfunction e.g hypotension.</p> <p>Management: Levo dopa + Carbidopa, D2 agonists, MAO inhibitors.</p> <ol style="list-style-type: none"> 1. Levo Dopa: combined with carbidopa (decarboxylase inhibitor) to prevent peripheral metabolism/degradation of dopamine. L-dopa should be started early with carbidopa and effectiveness of therapy decreases with time (usually 2-3 years). 2. D2 agonists: Bromocriptine, cabergoline, may cause pulmonary/retroperitoneal fibrosis. 3. MAO inhibitors: e.g., Phenylethylamine, Selegiline and tranylcypromide
Huntington disease	<ul style="list-style-type: none"> ○ Autosomal dominant, trinucleotide repeat expansion (CAG) in Huntington gene on chromosome 4 leads to atrophy of caudate + putamen with ex vacuo ventricomegaly (the compensatory inc in CSF spaces and volume because of brain atrophy/volume loss). ○ There is ↓ GABA, ↓ Ach, ↑ Dopamine. Neuronal death via NMDA-R binding and resultant glutamate toxicity because GABA balances glutamate. Loss of GABA → glutamate toxicity. ○ Clinical features: B/w age 20-50 with chorea, athetosis, dementia, aggression + depression. ○ The diseases have phenomena of Anticipation → early appearance of disease in successive generations with more severe symptoms and disease course.
Alzheimer disease	<ul style="list-style-type: none"> ○ Most common cause of dementia in elderly. Down's syndrome patients have early onset of it 35 yr. age because APP is located on 21st chromosome. ○ Disease is associated with altered proteins as follows. ○ Apo E4 → Inc risk in sporadic form, ApoE2 – dec risk in sporadic form, APP, Presenilin 1,2 ○ Morphology: Widespread cortical atrophy + narrowing of sulci and gyri → ↓ Acetylcholine ○ Mostly affected areas are Hippocampus and Entorhinal cortex in brain.

	<ul style="list-style-type: none"> Senile plaques in gray matter, Beta amyloid angiopathy (may cause hemorrhage), neurofibrillary tangles (intracellular hyper-phosphorylated tau protein), Hirano bodies - intra-cellular eosinophilic proteinaceous rods in Hippocampus. Aβ – Amyloid beta synthesized by cleaving amyloid precursors. Number of NF tangles correlate with degree of dementia. Treatment: Cholinergic drugs/Acetyl cholinesterase inhibitors: Donepezil, Rivastigmine, galantamine
Pick Disease	<ul style="list-style-type: none"> Also called Frontotemporal dementia due to marked atrophy of frontal + temporal lobes, swollen neurons and pick bodies – hyperphosphorylated tau protein (round cytoplasmic inclusions of neurofilaments). More common in Females. Disorder resembles Alzheimer disease but normal EEG and presents with early changes in personality and behaviour/aphasia.
Lewy body dementia	<ul style="list-style-type: none"> Dementia + visual hallucinations and fluctuating cognition, intracellular Lewy bodies in cortex, REM sleep behavior disorder. It is called Lewy body dementia if cognitive and motor symptoms onset < 1 year apart, otherwise it is called dementia secondary to Parkinson and managed by Rivastigmine. Diagnosis by single-photon emission computed tomography (SPECT) or DaT scan.
Vascular dementia	<ul style="list-style-type: none"> 2nd Most common cause of dementia in old age, stepwise decline in cognition with late onset memory impairment and multiple cortical/sub-cortical infarcts on CT/MRI as a result of multiple arterial infarcts or chronic ischemia.
HIV associated dementia	<ul style="list-style-type: none"> In advanced HIV infection → cognitive deficits, gait disturbance, irritability or depressed mood Diffuse gray matter + subcortical atrophy, microglial nodules with multi-nucleated giant cells.
Creutzfeldt-Jakob disease	<ul style="list-style-type: none"> Also known as Bowine spongiform encephalopathy (spongiform cortex without inflammation) May be transmitted by contaminated material (Corneal transplant), neurosurgical equipment. Prions (PrPc → PrPsc sheet) Beta pleated sheet resistant to protease – protein misfolding disorder Features: Rapidly progressive dementia (weeks to months), + startle myoclonus + ataxia. Diagnosis: EEG → Periodic sharp waves and on CSF exam → raised 14-3-3 protein in CSF. The disease is fatal.

DEMYELINATING & DYSMYELINATING DISORDERS

Multiple sclerosis (MS)

Autoimmune inflammation + demyelination of CNS (brain & spinal cord) with axonal damage. Mostly affects females, age 20 – 40 yrs. Relapsing and remitting is the common feature of MS.

Clinical features include: (Young patients present with sensory + visual findings)

- Charcot triad (SIN):** Scanning speech, incontinence (urinary), intranuclear ophthalmoplegia, nystagmus
- Sensory:** these symptoms last for weeks – **pins/needles and numbness, trigeminal neuralgia**
Lhermitte's syndrome – neck flexion precipitates the electric shock sensations down the spine,
- Visual:** Optic neuritis, Optic atrophy and intranuclear ophthalmoplegia (INO).
Acute optic neuritis (AON) → sudden painful unilateral vision loss + Marcus gun pupil (diagnosed by Swinging light reflex).
- Motor:** Spastic weakness in legs mostly, urinary incontinence and intention tremors.
- Symptoms may worsen with raised body temperature, such as hot bath/exercise.

Diagnosis: CSF examination, **MRI (gold standard)**, Fundoscopy

- CSF Exam:** Oligoclonal bands are diagnostic. Raised IgG + Myelin basic protein in CSF.
- MRI:** **gold standard, Periventricular plaques (Oligodendrocytes loss + reactive gliosis)**
Multiple bright hyperintense lesion in white matter on MRI brain.

Treatment: (No cure available, only diseases modifying therapies available).

- Acute flares:** Steroids (IV Methylprednisolone short course 03 – 05 days)
- Disease modifying agents: Natalizumab, Beta-interferon, mitoxantrone – for high frequency relapse.
- Pain relief:** By TCAs (Amitriptyline) or anti-convulsants (Pre-gablin/Gabapentin).
- Spasticity:** baclofen 1st line, alternate is gabapentin. 2nd line – diazepam/dantrolene or tizanidine (Tab Movax 2mg).
- Plasmapheresis:** in life-threatening relapses not resolving with other available drugs.

Acute inflammatory demyelinating polyneuropathy	<ul style="list-style-type: none"> Most common subtype of Gullian Baré syndrome, destroying Schwann cells by inflammation and demyelination of motor fibers, sensory fibers, and peripheral nerves (including CN III – XII) Despite association with infections, no definitive causal link to any pathogen. Triggered by stress/inoculation and facilitated by molecular mimicry (autoimmune). Features: Symmetric ascending paralysis + absent deep tendon reflexes beginning from lower limbs. Facial paralysis and respiratory failure are common. Arrhythmias, HTN/ low BP may occur. Most patient survive with good functional recovery. Diagnosis: CSF examination shows Albuminocytological dissociation i.e Raised CSF protein and normal cell count. EMG and Nerve conduction studies are also diagnostic. Management: No role of steroids, IVIG is preferred, and plasma exchange can also be done. Ventilatory support is essential.
Charcot-Marie Tooth disease (Autosomal dominant)	<ul style="list-style-type: none"> CMT/Hereditary motor and sensory neuropathy, most common type CMT1A caused by <i>PMP22</i> gene duplication, defective synthesis of proteins essential for peripheral nerves and myelin. CMT = Can't move toes, associated with foot deformities (Pes cavus), lower limb weakness/foot drop and sensory deficits.
Osmotic demyelination syndrome	<ul style="list-style-type: none"> Also called Central pontine myelinolysis syndrome – massive axonal demyelination in white matter of pons. Most common cause is iatrogenic correction of hyponatremia, other factor is rapid shift of solutes (e.g, glucose). Presents with acute paralysis, dysphagia, dysarthria, diplopia, and loss of consciousness. May result in locked-in syndrome. Correcting serum Na⁺ too fast: <ul style="list-style-type: none"> From high → low: your brain will blow (cerebral edema/herniation) From low → high: your Pons will die (osmotic demyelination syndrome)

HERNIATION SYNDROMES

- Cingulate/Subfalcine herniation:** May compress anterior cerebral artery
- Central/downward transtentorial herniation:** usually fatal due to caudal displacement of brainstem leading to rupture of paramedian branches of basilar artery. Duet hemorrhages are the multiple pinpoint bleeding spots due to herniation of brainstem.
- Uncus transtentorial herniation** leads to ipsilateral CN III palsy, contralateral paralysis, and coma (in late herniation)
- Cerebellar tonsillar herniation:** tonsillar herniation into foramen magnum → compresses brainstem and causes coma/death

NEUROCUTANEOUS DISORDERS		
Neurofibromatosis	Neurofibromatosis type 1 or (Von Recklinghausen disease)	Neurofibromatosis type 2
	Autosomal dominant mutation of NF1 tumor suppressor gene on chromosome 17 (normally NF1 is -ve RAS regulator).	Mutation of NF2 gene on chromosome 22 that codes for merlin . NF2 is also tumor suppressor gene.
	Cutaneous neurofibromas, Cafe-au-lait spots, Lisch nodules, optic gliomas , pheochromocytomas ,	Bilateral acoustic neuromas/vestibular schwannomas, juvenile cataracts, meningiomas and ependymomas.
Tuberous sclerosis	Autosomal dominant mutation is TSC 1 (Hemartin) or TSC 2 (Tuberin) Presents with Hamartomas in CNS and skin, Ash leaf spots , cardiac Rhabdomyomas , renal angiomyolipomas , Shagreen patches on skin of lumbar spine and seizures.	
Sturge-Weber syndrome	Congenital Non-hereditary anomaly of neural crest derivatives, somatic mosaicism of an activating mutation in copy of GNAQ gene. Presents with capillary vascular malformation → Port-wine stain in CN V1/V2 distribution – (non-neoplastic birth mark), Glaucoma , epilepsy, mental retardation and tram-track calcifications.	
Von Hippel- Lindau disease	Autosomal dominant deletion of VHL gene on chromosome 3p. pVHL = Hypoxia inducible factor 1 a, leads to numerous benign and malignant tumors as follows;	

Bilateral RCC, pheochromocytomas, Hemangioblastomas in retina, cerebellum, brain stem and spine. Hemangioblastomas → inc. EPO production.

KEY FACTS -- NEURODEGENERATIVE, DEMYELINATING AND NEURO CUTANEOUS DISORDERS

1. Cog wheel Rigidity, Pill roll tremors, bradykinesia, shuffling gait, low Dopa and Lewy bodies = Parkinsonism, treat with D2 agonists (Bromocriptine/Cabergoline).
2. Atrophy of Caudate ± putamen, Chorea, athetosis, dementia, aggression + depression, low GABA, high Dopa, Anticipation, CAG repeats = Huntington disease (AD, chromosome 4 involved).
3. Old age dementia, neurofibrillary tangles, Hirano bodies, early onset in Down's syndrome, Apo E4, Apo E2, wide-spread cortical atrophy, low Ach, Aβ amyloid, treated with rivastigmine = Alzheimer's disease.
4. Female with dementia, fronto-temporal atrophy, pick bodies, behavior/personality changes = Pick disease.
5. Dementia + visual hallucinations, cognitive and motor symptoms within 01 yr., Lewy bodies = Lewy body dementia.
6. Post-stroke memory alterations in old age with sub-cortical/cortical infarcts on MRI = Vascular dementia.
7. History of HIV/AIDS, Memory and behavioural changes, gait disturbance = HIV associated dementia.
8. Corneal transplant, spongiform cortex, raised 14-3-3 protein in CSF, Beta pleated sheet = Creutzfeldt-Jakob disease.
9. Female 20-30 yr., numbness tingling sensation in limbs, Vision loss, Scanning speech, urinary incontinence, spasticity, Oligoclonal band in CSF, Periventricular plaques MRI (gold standard), oligodendrocytes loss = Multiple sclerosis.
10. History of Diarrhea with Campylobacter jejuni, ascending paralysis beginning from lower limbs, loss of DTRs, Albuminocytological dissociation in CSF, Treated by IVIG = GBS (Acute inflammatory demyelinating polyneuropathy).
11. PMP 22 gene duplication, sensory and motor deficits, foot/toe abnormalities + weakness = Charcot Marie tooth disease
12. Correcting serum Na too fast in hyponatremia, dysphagia, dysarthria, diplopia = Central pontine myelinolysis.
13. Autosomal dominant Mutation of NF1 gene (neurofibromin) on chromosome 17, Cutaneous neurofibromas, Cafe-au-lait spots, Lisch nodules, optic gliomas, pheochromocytomas = Von Recklinghausen disease /NF 1.
14. Mutation of NF2 gene (merlin) on chromosome 22. Bilateral acoustic neuromas/vestibular schwannomas, juvenile cataracts, meningiomas and ependymomas = Neurofibromatosis type 2
15. Autosomal dominant mutation in TSC 1 (Hamartin) or TSC 2 (Tuberin), ash leaf spots, cardiac Rhabdomyomas, renal angiomyolipomas =, Tuberous sclerosis
16. Port wine stain (birth mark), glaucoma, mutation of GNAQ gene, mental retardation = Sturge-Weber syndrome
17. Autosomal dominant deletion of VHL gene on chromosome 3p. pVHL = Hypoxia inducible factor 1 a, Bilateral RCC, pheochromocytomas, Hemangioblastomas in retina, cerebellum, increase EPO production = Von Hippel- Lindau disease. (VHL disease)

TUMORS OF CNS

1. Most tumors are intracranial; tumors of the spinal cord are much less frequent.
2. In adults, most intracranial tumors are Supratentorial.
3. In children, most intracranial tumors are Infratentorial.
4. CNS tumors are the second most common form of malignancy in children (only leukaemia is More frequent).
5. Primary malignant CNS tumors rarely metastasize.
6. Benign intracranial tumors can result in devastating clinical consequences due to compression Phenomena.
6. **Metastatic tumors to the brain are found more frequently than primary intracranial neoplasms.**
7. Most common **primary** intracranial tumors in adults are-glioblastoma Multiforme > meningioma > acoustic neuroma
8. Childhood pilocytic astrocytoma is most common tumor in children overall.
9. Medulloblastoma is most common malignant tumor in children (especially < 05 years of age)

CLASSIFICATION

1. Gliomas → Astrocytomas, Oligodendroglioma, Ependymomas.
2. Non-glial tumors → Craniopharyngioma, Schwannoma, Meningioma, Lymphoma, Hemangioblastomas
3. Primitive Neuroectodermal origin (PNET): Medulloblastoma
4. Metastatic tumors: most common brain tumor overall (Not primary tumors)

<u>Astrocytomas</u>	<ul style="list-style-type: none"> Most common Primary brain tumor, +ve for glial fibrillary acidic protein (GFAP). Divided based on their infiltration into surrounding brain parenchyma (WHO classification) <p>WHO Grade I: They Do not infiltrate, examples are: Pilocytic astrocytoma, pleomorphic xanthoastrocytoma and subependymal giant cell astrocytoma.</p> <p>Pilocytic astrocytoma: most common primary brain tumor in children, mostly in Posterior cranial fossa involving cerebellum. Well circumscribed, Benign Solid/cystic mass, GFAP +ve, Bipolar cells with hair like projections, Association with microcysts + Rosenthal fibers.</p> <p>▪ WHO Grade II: Low grade fibrillary astrocytoma</p> <p>▪ WHO Grade III: Anaplastic astrocytoma</p> <p>▪ WHO Grade IV: Glioblastoma Multiforme (GBM is actually grade IV astrocytoma) Glioblastoma Multiforme: most common malignant brain tumor in adults (old age). Grade IV, GFAP +ve, association with EGFR amplification + PTEN mutation, found in cerebral hemispheres, crosses midline/corpus callosum hence called Butterfly glioma Highly aggressive and malignant → marked anaplasia and pleomorphism. Pseudopalisading pleomorphic tumor cells, necrosis, and hemorrhage ± capillaries proliferation, very poor prognosis with survival rate only 01 year to 15 months.</p>
<u>Oligodendroglioma</u>	<ul style="list-style-type: none"> Rare, slow growing tumor in Middle Ages typically involving frontal lobes. Foci of calcifications, Fried egg cells (round large nuclei with clear halo of cytoplasm), Chicken – wire capillary pattern.
<u>Ependymoma</u>	<ul style="list-style-type: none"> May occur in both children and adults in 4th ventricle arising from ependymal cells. Poor prognosis and may cause Hydrocephalus. Tumor cells demonstrate blepharoblasts – rod shaped structured representing basal bodies of cilia, tubules or rosettes with cells encircling vessels or pointing towards central lumen.
<u>Medulloblastoma</u>	<ul style="list-style-type: none"> Most common malignant brain tumor in childhood arising from cerebellum. Form of primitive neuroectodermal tumor – Synaptophysin +ve. Tumor mass may: Compress cerebellum → ataxia, compress 4th ventricle → obstructive hydrocephalus or Send drop metastasis to spinal cord. Associated with Turcot syndrome = medulloblastoma, GBM, GIT polyps, colorectal cancer. Histology reveals sheet of small blue closely packed cells with scant cytoplasm arranged in Homer Wright rosette or Perivascular pseudorosette pattern.
<u>Meningioma</u>	<ul style="list-style-type: none"> A predominantly benign tumor arising from Arachnoid cells, 2nd common brain tumor in adults, more in Females, relation with progesterone levels, T tumor size in menstrual cycle. The tumor is outside the brain and can be removed surgically. Most frequent sites are convexities of cerebral hemi-spheres, parasagittal region, falx cerebri, sphenoid ridge. Histology shows whorled pattern of concentrically arranged spindle cells and laminated calcifications Psammoma bodies. Variants or grades are as follows: Grade I: Benign, slow growing – most cases are grade I. Grade II: Clear cell and choroid variants Grade III: Papillary and rhabdoid variants. These are aggressive variants.
<u>Craniopharyngioma</u>	<ul style="list-style-type: none"> Most common childhood Supratentorial tumor arising from remnants of Rathke pouch (ectoderm). Calcification is common, Cholesterol crystals found in motor-oil like fluid within tumor, high recurrence rate, may cause bitemporal hemianopia – confused with pituitary adenoma.
<u>Schwannoma</u>	<ul style="list-style-type: none"> arising from Schwann cells, S-100 +ve, classically found at cerebello-pontine angle – benign involving CN V, VII and VIII but can be along any peripheral nerve. When involves cranial nerve VIII → acoustic neuroma (3rd common intracranial tumor) may present with sensorineural hearing loss especially in old age. Bilateral schwannomas are found in NF2. Histology: biphasic, dense hypercellular areas having spindle cells alternating with hypo-cellular myxoid areas. One of given 2 patterns can be found: <ol style="list-style-type: none"> Antoni A: hypercellular, elongated cells with palisading nuclei

	2. Antoni B: looser, hypocellular pattern (myxoid) Tumor can be resected using stereotactic radiosurgery.
Pituitary adenoma	<ul style="list-style-type: none"> May be hyperfunctioning (hormone production) or non-functioning/silent causing mass effects e.g bitemporal hemianopia. Most common is from Lactotrophs (Prolactinoma) → amenorrhea, galactorrhea, loss of libido. Treat with D2 agonists such as Bromocriptine or cabergoline. Less commonly from ▪ Somatotrophs (GH producing) → acromegaly, gigantism or ▪Corticotrophs – Cushing disease, Rarely from Thyrotrophs (TSH)/gonadotrophs (FSH, LH).
Pinealoma	<ul style="list-style-type: none"> Tumor of pineal gland may cause Parinaud syndrome → vertical gaze palsy by compression of tectum, obstructive hydrocephalus, precocious puberty in males (HCG production). It is like germ cell tumor of testes (seminoma)
Hemangioblastoma	<ul style="list-style-type: none"> Blood vessels origin, closely arranged thin walled capillaries with minimal intervening parenchyma, mostly arises in cerebellum and associated with Von-Hippel Lindau syndrome. Produces EPO and may cause secondary Polycythemia.
Metastatic tumors	<ul style="list-style-type: none"> More common than primary tumors. They originate most frequently from following sites: Lungs > Breast > skin > kidney > GIT > Thyroid.

BRAIN TUMORS

- Adult Brain Tumors**
 - MALIGNANT**
 - BRAIN METASTASES**
Lung, Breast, Melanoma
 - HIGH-GRADE GLIOMAS**
ASTROCYTIC
Glioblastoma, Astrocytoma
 - OLIGODENDROGLIAL
Oligodendroglioma
 - BENIGN**
 - MENINGIOMA
 - PITUITARY ADENOMA
- Childhood Brain Tumors**
 - MALIGNANT**
 - EMBRYONAL**
Medulloblastoma
 - ASTROCYTIC**
Diffuse midline glioma
Glioblastoma
 - BENIGN**
 - ASTROCYTIC**
Pilocytic Astrocytoma
SEGA
 - EPENDYMAL**
Ependymoma
Subependymoma

MALIGNANT BRAIN TUMORS**Adults****BRAIN METASTASES****MOST COMMON**

- Lung (~50%), Breast, Melanoma, G.I., Renal cell

HIGHEST RISK OF HEMORRHAGE

- Melanoma, Renal cell

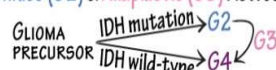
MALIGNANT GLIOMAS

- Glioblastoma (GBM), G4**

Pseudopalisading necrosis

Butterfly glioma

- Diffuse (G2) & Anaplastic (G3) Astrocytoma**



- Oligodendroglioma, G2, G3**

Fried-egg cell appearance

1p/19q co-deletion

CNS LYMPHOMA (B-CELL LYMPHOMA)

- Primary CNS Lymphoma (PCNSL)**

When assoc. w/HIV, EBV is +

- Secondary CNS Lymphoma**

Children**MALIGNANT GLIOMA**

- Diffuse midline glioma, G4**

H3 K27M-mutant

- Glioblastoma (GBM), G4**

EMBRYONAL TUMOR

- Medulloblastoma, G4**

Small blue cells, Homer Wright rosettes

- Atypical teratoid/rhabdoid tumor (ATRT), G4 (Infants < 3 y.o.)**

BENIGN BRAIN TUMORS**Adults****MENINGIOMAS**

- Meningioma, G1**

Whorls

- Psfammoma bodies**

PITUITARY TUMORS

- Pituitary adenoma, G1**

Macro > 10mm, Micro < 10mm

Prolactin, Growth H., ACTH

Children**EPENDYMAL TUMORS**

- Ependymoma, G2**

Perivascular Pseudorosettes

vs. Subependymoma, G1

ASTROCYTIC

- Pilocytic astrocytoma, G1**

- SEGA, G1 (Tuberous sclerosis)**

SELLAR REGION

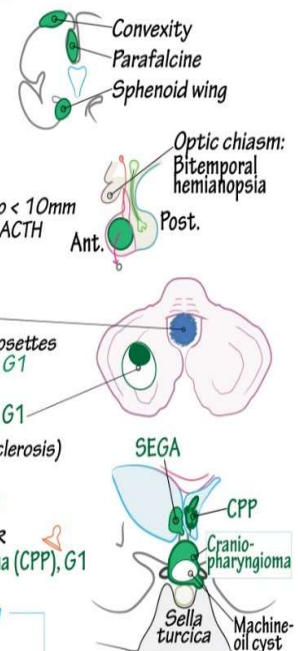
- Craniopharyngioma, G1**

CHOROID PLEXUS TUMOR

- Choroid plexus papilloma (CPP), G1**

WHO GRADING SYSTEM

- G1**
 - Low proliferation
 - Well circumscribed
- G2**
 - Low proliferation
 - Potential for infiltration
- G3**
 - High proliferation
 - Highly infiltrative
- G4**
 - High proliferation
 - Necrosis/Neovascularity
 - Infiltration/dissemination

**U.S. BRAIN TUMOR INCIDENCE**

Brain Metastasis	~ 150k
Primary Brain Tumors	~ 75k
Meningiomas	35%
Glioblastomas	16%
Pituitary tumors	15%
Gliomas (non-GBM)	10%

Clinical features:

- Generally, depends upon the part of brain they involve. Morning Headache with vomiting, seizures, memory deficits, behavioral or personality changes. Seizures are common with frontal lobe tumors.
- Hydrocephalus with Medulloblastoma or Ependymoma/pilocytic astrocytoma.
- Weakness, sensory abnormalities, ataxia
- Facial palsy + hearing loss, tinnitus, balance disturbance seen in **Cerebello-pontine** angle tumors.

Investigations and Management:

- MRI – investigation of choice. Others are CT brain, biopsy, and PET scan.
- Treated with surgical resection (meningioma), trans-sphenoidal resection for pituitary adenomas.
- Chemotherapy and radiotherapy can also be done.

MOTOR NEURON DISEASES (MNDs)	
Amyotrophic lateral sclerosis (ALS)	<ul style="list-style-type: none"> • ALS is also known as Lou Gehrig disease. Most common form of MND is ALS. • Degeneration of both upper and lower motor neurons is characteristics. • No sensory or bowel/bladder deficits. • Degeneration + atrophy of lateral corticospinal tract + anterior motor neurons of spinal cord → denervation atrophy of musculature. • ALS Presents in early middle age (20-30 years of age) with rapid course leading to death from respiratory failure mostly in 1-6 years. The clinical features are: • UMN signs – hyperreflexia, spasticity, inc. Tone, pseudobulbar palsy • LMNL signs – symmetric atrophy + fasciculations, bulbar palsy • Treatment: Riluzole
Other forms of MND	<ul style="list-style-type: none"> • Progressive bulbar palsy and infantile progressive spinal muscle atrophy. • Spinal muscular atrophy → congenital degeneration of anterior horn cells --LMN s symptoms only (hypotonia – floppy baby, Tongue fasciculations, flaccid paralysis. • Defective sRNP assembly is the likely pathogenesis.

SPINAL CORD LESIONS & CNS INFECTIONS -- SUMMARY	
Cauda equina syndrome	<ul style="list-style-type: none"> ○ Compression of spinal roots L2 and below due to intervertebral disc herniation or tumor. ○ Radicular pain, absent knee and ankle reflexes, loss of bowel (anal sphincter) and bladder tone, saddle anaesthesia.
Brown – Séquard syndrome	<ul style="list-style-type: none"> ○ Hemisection of spinal cord. Clinical features are: ○ At level of lesion: ipsilateral loss of all sensation + ipsilateral LMN signs (flaccid paralysis). ○ Below level of lesion: ○ ipsilateral UMN signs (due to corticospinal tract damage) + ipsilateral loss of light touch or 2-point discrimination, vibration, proprioception ○ Contralateral loss of pain, temperature, and crude touch below the level of lesion due to contralateral Spinothalamic tract damage. ○ If lesion occurs above T1 → additional feature, ipsilateral Horner syndrome due to damage of oculosympathetic pathway. ○ So, in Brown Séquard syndrome every sensory/motor loss is ipsilateral except pain, crude touch and temperature (contralateral loss).
Syringomyelia	<ul style="list-style-type: none"> ○ Syring (fluid-filled cyst) forms that expands and damages anterior white commissure of Spinothalamic tract (2nd order neurons), it leads to Bilateral symmetrical loss of pain and temperature in cape-like fashion. Fine touch is preserved. ○ Most common location: Cervical > Thoracic > Lumbar ○ Also seen in Arnold Chiari 1 malformation.
Tabes dorsalis	<ul style="list-style-type: none"> ○ Caused by Tertiary syphilis, degeneration/demyelination of dorsal columns and roots. ○ Progressive sensory ataxia (impaired proprioception), +ve Romberg sign and absent DTRs. ○ Association with Argyll-Robertson pupil and Charcot joints.
Poliomyelitis	<ul style="list-style-type: none"> ○ Polio virus -- feco-oral route, destruction of cells in anterior horn of spinal cord (LMN death). ○ Signs of LMNL: Asymmetric weakness of limbs, flaccid paralysis, hyporeflexia, fasciculations. ○ Virus can be detected in Stool or throat. CSF shows inc Lymphocytes and slightly ↑ protein
Vit B12 deficiency	<ul style="list-style-type: none"> ○ Subacute combined degeneration: ○ demyelination of lateral CST, dorsal columns, and spinocerebellar tracts ○ Presents with ataxic gait, paraesthesia, impaired position/vibration sense -- +ve Romberg sign ○ UMN symptoms may be present.
Friedrich Ataxia	<ul style="list-style-type: none"> ○ Autosomal recessive, trinucleotide repeat extension (GAA)_n for frataxin gene on chromosome 9.

	<ul style="list-style-type: none"> Leads to impaired mitochondrial functioning. Damage to lateral CST, DCML, DRG and spino-cerebellar tract → staggering gait, frequent falling, nystagmus, dysarthria, pes cavus, diabetes mellitus, childhood Kyphoscoliosis. HOCM is the cause of death.
CNS infections	<ul style="list-style-type: none"> Brain Abscess: may be multiple or single. No Lymphatic enters the brain and most common route of CNS infection is Hematogenous in Frontal > Temporal lobe Most common source for single abscess, from contiguous sites → Otitis media/middle ear inf Multiple abscess is due to Bacteraemia. Most common organism are S. Aureus and Viridians streptococci (history of dental infection). Ring enhancing lesion on CT brain indicates brain abscess. Other infections: Meningitis (streptococci, H.infl/N.meningitidis) or Tuberculous meningitis. Toxoplasmosis (paraventricular/basal ganglia calcifications), Herpes simplex encephalitis, CMV encephalitis
Spinal shock vs Neurogenic shock	<ul style="list-style-type: none"> Spinal shock: injury to spinal cords leads to immediate transient loss of all reflexes, sensations below level of lesion, paraplegia or quadriplegia, hypotension, bradycardia, loss of bulbocavernosus reflex, the reflexes may return after few times. Neurogenic shock: loss of sympathetic or vasomotor tone → vasodilation -- hypotension, bradycardia, Warm dry skin. Injury occurs specifically at or above T5/T6 level.

CONGENITAL MALFORMATIONS OF CNS

Neural tube defects (NTDs)	<p>Neuropores fail to fuse by the 4th week of development → persistent connection between amniotic cavity and spinal canal. Associated with diabetes and folate deficiency during pregnancy.</p> <p>↑ alpha fetoprotein (AFP) in amniotic fluid and serum (except spina bifida occulta = normal AFP).</p> <p>↑ acetylcholinesterase (AChE) in amniotic fluid is a helpful confirmatory (most specific) test.</p> <hr/> <p>Spina bifida Occulta: Failure of caudal neuropore to close, but no herniation. Usually seen at lower vertebral levels. Dura is intact.</p> <p>Associated with tuft of hair or skin dimple at level of bony defect.</p> <hr/> <p>Meningocele: Meninges (but no neural tissue) herniate through bony defect.</p> <hr/> <p>Myelomeningocele: Meninges + neural tissue (eg, cauda equina) herniates through bony defect.</p> <hr/> <p>Myeloschisis/rachischisis: Exposed, unfused neural tissue without skin/meningeal covering.</p> <hr/> <p>Anencephaly: Failure of rostral neuropore to close - no forebrain, open calvarium, frog eye sign. Clinical findings: Polyhydramnios (no swallowing center in brain).</p>
Chiari I malformation	Associated with Syringomyelia, ectopia of cerebellar tonsils inferior to foramen magnum, usually asymptomatic in childhood but may present with headache and cerebellar symptoms in adults.
Chiari II malformation	More severe than Chiari I and presents early in life, usually associated with cerebral aqueduct stenosis and Meningomyelocele of lumbosacral region. Herniation of Cerebellar tonsils + medulla through foramen magnum may lead to non-communicating hydrocephalus. Other features include sensory loss at/below level of lesion if linked with Myelomeningocele.
Dandy walker malformation	Agenesis of cerebellar vermis → cystic enlargement of 4 th ventricle. Association with non-communicating hydrocephalus and spina bifida.

Clinical reflexes	<p>Superficial reflexes: Polysynaptic, elicited by sensory stimulus to skin e.g Superficial abdominal reflexes and cremasteric reflex</p> <p>Deep Reflexes/Deep tendon reflexes (DTRs): monosynaptic, elicited by action on muscles (not skin).</p> <p>Grading of Reflex: 0 = absent, 1 = hypoactive, 2 = normal, 3 = hyperactive, 4 = clonus</p> <p>■ Achilles reflex /Ankle Jerk → S1, S2 ■ Patellar reflex/Knee jerk → L3-L4 (L3 main).</p> <p>■ Biceps and brachioradialis reflexes → C5, C6 ■ Triceps reflex → C6, C7, C8</p> <p>■ Cremasteric reflex → L1, L2. ■ Anal reflex → S3, S4</p>
Primitive reflexes	<p>Moro reflex: hang on for life reflex – abduct/extend arms when startled and then draw together. It disappears by 6 months postnatally.</p> <p>Plantar reflex: Dorsiflexion of big toe + fanny of other toes upon plantar stimulation. Normally present till 01 year post-natal. In adults' presence or this reflex indicates → Babinski sign +ve – signify the UMN. In infants it is normal due to ongoing myelination of corticospinal tracts (not completed).</p> <p>Palmar reflex: stroking the palm causes curling of fingers.</p> <p>Rooting reflex: upon stroking cheek (nipple seeking) or arm → movement of head towards one side</p>

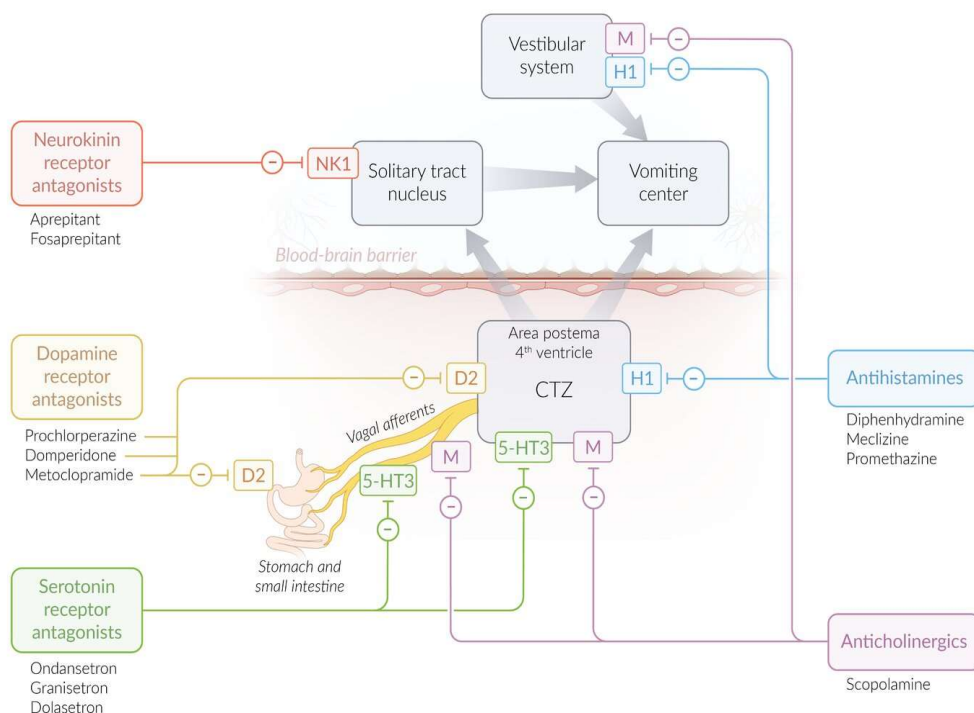
	<p>Suckling reflex: sucking response when roof of mouth is touched.</p> <p>Galant reflex: stroking one side of spine → lateral flexion of lower body towards side of stimulation when newborn is in ventral suspension/face down.</p> <p>■ Primitive reflexes are present in healthy infants but absent in neurologically intact adult. They normally disappear in 1st year of life. They are inhibited by a mature or developing frontal lobe. They may remerge in adult life due to Lesion of frontal lobe → loss of inhibition of primitive reflexes.</p>
ABNORMAL MOVEMENTS	
Tremors	<p>Essential tremors → often familial, high frequency tremors with sustained posture e.g outstretched hands and worsened by anxiety or movement. Treated with Propranolol.</p> <p>Resting tremors → occur at rest e.g Pill rolling tremors of Parkinson disease. Uncontrolled movement of distal limbs (e.g hands) and tremors alleviated by intentional movement.</p> <p>Intention tremors → slow, zig-zag motion when pointing toward a target in cerebellar lesion.</p>
Dystonia	Sustained involuntary muscle contractions (writer's cramp, blepharospasm, torticollis). Treated by Botox (botulinum toxin) injection.
Akathisia	Restlessness and intense urge to move seen with antipsychotic drugs usage (neuroleptics) or side effect of Parkinson treatment.
Asterixis	Wrists extension causes flapping motion, seen in hepatic encephalopathy and Wilson disease.
Myoclonus	Sudden brief uncontrolled muscle contraction e.g Jerks/hiccups. Common in metabolic abnormalities linked with renal/liver disease.
Restless legs syndrome	Uncomfortable sensation in legs causing irresistible urge to move them and relived by movement Worst at rest/night. Associated with CKD or iron def anemia. Treat with Dopamine agonists e.g pramipexole/Ropinirole.
Chorea	Sudden jerky purposeless movements in caudate lesion, e.g seen in Huntington disease.
Athetosis	Slow Writhing movement of hands in globus pallidus lesion.
Hemiballismus	Sudden wild flailing of one side of the body in contralateral subthalamic nucleus lesion.

NEUROTRANSMITTERS	
Types	<ol style="list-style-type: none"> Excitatory: Glutamate (major excitatory + for fast pain), aspartate, Nitric oxide (vasodilator). Inhibitory: GABA (Major inhibitory), Glycine, Dopamine, serotonin Both: acetylcholine, nor-epinephrine.
Changes with disease	<ul style="list-style-type: none"> Anxiety: ↓ GABA, ↓ Serotonin, ↑ Norepinephrine. Depression: ↓ Serotonin, ↓ Dopamine, ↓ NE. Parkinson disease: ↓ Dopamine, ↑ Ach Huntington disease: ↓ GABA, ↑ Dopamine, ↓ Ach Alzheimer disease: ↓ Acetylcholine Schizophrenia: ↑ Dopamine
VOMITING (Center, Receptors, Mechanism) + ANTIEMETICS	

- Coordinated by nucleus tractus solitarius (NTS) in the medulla, which receives information from the
- Chemoreceptor trigger zone (CTZ, located within area postrema in 4th ventricle)
- GI tract (via vagus nerve), vestibular system, and CNS.
- CTZ and adjacent vomiting center nuclei receive input from 5 major receptors:
- muscarinic (M1), Dopamine (D2), histamine (H1), serotonin (5-HT3), and neurokinin (NK-1) receptors.
- 5-HT3 D2, and NK-1 antagonists used to treat chemotherapy-induced vomiting.
- H1 and M1 antagonists treat motion sickness
- H1 antagonists treat hyperemesis gravidarum.
- Mechanism of vomiting:** Stimulus (sight/smell/meningeal irritation/GI stimulation) → inc salivary glands fluids → deep breath (to avoid respiration) → GI retroperistalsis (pyloric sphincter + lower Esophageal relaxation) → vocal cords adduction – dec intrathoracic pressure against closed glottis → retching → vomiting.

Drug of choice

1. Motion sickness	Scopolamine (Muscarinic antagonist) , cyclizine
2. Morning sickness	Pyridoxine
3. Mountain sickness	Acetazolamide
4. Air sickness.	Meclizine



Type	Distribution
Afferent	
General somatic afferent (GSA)	Skin, skeletal muscles, joints, and bones.
General visceral afferent (GVA) (Autonomic afferent)	Visceral organs
Special somatic afferent (SSA)	Retina, auditory and vestibular organs i.e., eye & ear.
Special visceral afferent (SVA)	Gustatory and olfactory receptors i.e., tongue & nose.
Efferent	
General somatic efferent (GSE)	Skeletal muscles from somites.
General visceral efferent (GVE) (Autonomic efferent)	Smooth muscles and glands.
Special visceral efferent (SVE)	Skeletal muscles from pharyngeal arches e.g., 1 st arch muscles.

PAST PAPERS BCQs – ONE LINERS

1. Fast conduction in myelinated fibers due to = Saltatory conduction.
2. EEG of a man with relax mind and eyes closed show which EEG waveform = Alpha waves.
3. Part of brain involved in; intelligence is = frontal lobe.
4. Preganglionic sympathetic nervous system supplies = Adrenal medulla
5. Anterior hypothalamus maintains temp effectively by = Cutaneous vasodilation.
6. Deep sleep is characterized by = Delta waves.
7. If temperature of set point increase, then there will be decreased in = sweating.
8. Which receptor senses vibration = Pacinian – High frequency vibration.
9. Low frequency vibration detected by which of these = Meissner
10. Decrease core body temperature what will be stimulated = shivering.
11. Theta wave will appear in which of following stage of sleep = NREM 3
12. Neuron from substantial nigra pars compacta to striatum is = Dopaminergic.
13. Alpha Rhythm on EEG increase frequency sue to = Low glucocorticoids
14. Low PCO₂ will cause which of following effect = Decrease Cerebral blood blow.
15. Clasp knife reflex is exaggerated response of = Golgi tendon.
16. Only afferent nerve that carries information to the brain = Optic.
17. Nucleus of REM sleep is = locus cerulus (in Pons)
18. Which of the following mechanism prevent heat loss = Vasoconstriction.
19. Deep sea diver ascends suddenly to surface which toxicity will occur and cause death = seizure.
20. Man got an accident and had complete transection at T1 level he will have = Temporary loss of stretch reflex below the lesion.
21. In voluntary contraction, descending pathways cause excitation of = Both alpha and gamma motor neuron discharge.
22. Disequilibrium response of autonomic nervous system shown in which of following = Meniere's disease.
23. Which of the following is slow adapting receptor = Ruffini receptor.
24. Forceful stretching of muscle is done which of the following prevent muscle tear = Golgi spindle.
25. The amount of heat loss from body depends upon = Temperature of external environment.
26. Which of the following is released at the synapse between incoming pain fibers and pain inhibitory fibers in spinal cord = Enkephalin.
27. How anterior hypothalamus regulates temperature = By sweating and vasodilation.
28. Neurotransmitter of mood is = Serotonin.
29. The strongest inhibitory signal in CNS comes from which neuron = Purkinji cells of cerebral cortex.
30. Regarding microglial cells true is = Start activity in inflammatory response.
31. A naked person in AC with temperature 21, humidity 80 % and heat loss will be through= Radiation and conduction.
32. Decrease in which neurotransmitter cause anxiety = GABA.
33. A man while walking accidentally lands his foot on a pointed object and immediately removed it. Which of the following is involved in withdrawal reflex = Multisynaptic receptor.
34. Neurotransmitter of basal ganglia output is = GABA.
35. Bipolar neuron has how many dendrites = 01 (also 1 axon)
36. About astrocytes action potential what is true = Action potential is generated with increase extracellular potassium.
37. Seizures activity result of agent who block cerebral synaptic action of which= GABA.
38. Climber at high altitude experience hypothermia in returning to base camp generation due to which of following= Posterior hypothalamus.
39. Norepinephrine is released by = Postganglionic parasympathetic nerve fibers.
40. When temp of skin reaches 52 degree which receptors are stimulated = Nociceptors.
41. About parasympathetic true is =Pupil constriction.
42. Physiological indirect activity of brain = Pupillary reaction.
43. Micro glial cells in CNS= Are macrophages of CNS.
44. Chronic cold adaptation occurs through which one of the following mechanisms= Formation thermogenesis.
45. Cerebral oxygen metabolic rate = 3-4 ml/min/100g
46. REM sleep is characterised by = loss of muscle tone.
47. Sweat gland and piloerector muscles are supplied by = Cholinergic postganglionic sympathetic.
48. Withdrawal reflex carried by = Free nerve endings.
49. Neuroendocrine response involves which part = Hypothalamus.

50. Cushing reflex is initiated by = increase BP (in TBI/Head injury due to raised ICP)
51. The central temperature regulation occurs in = Anterior hypothalamus.
52. Hormone exhibit relation between weight and puberty =Leptin.
53. Vomiting centre located = Medulla (CTZ – Area Postrema)
54. Slow pain and Itching is carried by which fibers = C fibers
55. Which of the following receptors are with no adaptation =Pain receptors.
56. Bipolar cells found in = Olfactory neuron.
57. If temperature of set point increase, then there will be increase in = Shivering
58. Most abundant cells in white matter of CNS is = Oligodendrocytes.
59. What type of receptor is present in adrenal medulla = Nicotinic cholinergic.
60. Sympathetic cholinergic discharge occurs in = Sweat glands.
61. Which of the following occurs due to parasympathetic stimulation = Bronchoconstriction.
62. Taste pathway relay in = tractus solitarius (NTS).
63. Regarding thermo receptor= Long receptive field.
64. Brain metabolite is = CO ₂ .
65. Hormone which increases in darkness= Melatonin.
66. Neurohypophysis contain secretory granules stored in = Nerve stored in.
67. Absorption of CSF occurs in = Arachnoid granulation.
68. CSF differs from plasma in decrease = Protein and glucose (protein is more deficient).
69. Maximum concentration in vitreous humour is of = water.
70. Common astrocyte cells in gray matter = Protoplasmic astrocytes.
71. Basal ganglia released = GABA.
72. Density of CSF= 1.0005.
73. Herring Beurer reflex activated by = stretch receptors.
74. A patient with hypertonic arm increase sensitivity to muscle spindle flexor muscles stimulated initial resistance than flexed by mechanism = Increase Myotatic.
75. Person sitting in well-ventilated room having sweating tachycardia most likely due to = Mental Stress.
76. A Person working in a room having sweating tachycardia most likely due to = Exercise
77. Erection and decrease muscle tone occur at = REM.
78. Which nerve fibre carries touch and pressure sensation =A beta
79. Part of brain involved in REM sleep = Reticular formation.
80. Which type of nerve fibre has fast speed = Alpha – fibre (A – alpha fastest)
81. Connective tissue cells are derived from= Mesoderm.
82. Satiety and feeding centre location in = Hypothalamus.
83. What is true about sympathetic nervous system= Preganglionic fibres release acetylcholine.
84. Myelin sheath in the CNS is formed by = Oligodendrocyte.
85. Cause of increase blood flow to brain = CO ₂ > Acidosis.
86. Ventricles and central canal lined by = Ependymal cells.
87. Fast pain fiber is =A delta.
88. Pointed object touches foot sudden withdrawal which is appropriate= Multisynaptic.
89. 512Hz tuning fork placed over head of patient. Receptors involved= Pacinian.
90. Which of following is sympathetic effect= Bronchodilation via β_2
91. Pointed object touched to foot sudden withdrawal reflex = Multisynaptic/Polysynaptic.
92. Myelin sheath damage what effect occurs = Membrane resistance of nodal and internode.
93. Preganglionic sympathetic release = Acetylcholine.
94. Flexor reflex is carried by = Noxious stimulus.
95. Iggo dome receptors is collection of = Merkel disc.
96. Metabolic fuel of brain is = Glucose.
97. Muscle spindle acts through= Alpha motor neuron.
98. NMJ Neurotransmitter is= ACH.
99. Immediate effect in cold = Piloerection.
100. Cerebral perfusion pressure is equal to MAP When = dura is opened.
101. CSF pressure of water= 60mm.
102. Nociceptor located in = Meninges.

103.CSF composition is = Glucose lowers in CSF.
104.CSF specific gravity= 1.005- 1.009
105.Nerve metabolism is blocked by = Cyanide.
106.Heat loss is controlled by = Preoptic area. Athlete maximum heat loss through = Sweating.
107.Melatonin regulates which of the following = Pigmentation.
108.Which of the following is the effect of catecholamines after injury = Vasoconstriction.
109.0.5 gram/dl protein is present in which fluid = Lymph.
110.Fastest control of blood pressure is achieved by = Baroreceptors.
111.Local anaesthetic affects which of the following fibers = C Fibers.
112.Visual accommodation involves = Contraction of ciliary muscle to see nearby.
113.Heat loss in humid environment is through which of the following = Convection
114.When looking to near object what will increase = Parasympathetic on ciliary
115.When light strikes the eye what happens = Increase conversion of cis retinal to all trans retinal
116.Cochlear action potential is generated by = K ⁺ Influx into cells
117.Aqueous humor is produced by = Non pigmented ciliary epithelium
118.Which of the following statements regarding sympathetic and parasympathetic preganglionic is true = cholinergic.
119.What will be shows on electroencephalograph of an anaesthetic patient =Low waves.
120.Parasympathetic act on SA effect via which neurotransmitters = ACH.
121.Sympathetic beta-adrenergic effect on heart is = increase contractility of heart.
122.Hypophyseal structure receiving signals from hypothalamus via hypophyseal portal system = Adenohypophysis.
123.Grasp reflex in babies is present up to = By the end of 6 th postnatal month.
124.Receptor present on fingertips = Meissner corpuscle.
125.Most rapidly adapting receptors = Pacinian > Meissner.
126.First & important sign of cholinergic overdose = Bradycardia.
127.Which is not related to pain transmission =Hypothalamus.
128.Decrease sympathetic outflow leads to shock due to = Decrease vasomotor tone – Neurogenic shock
129.In voluntary contraction, descending pathways cause excitation of = Both alpha and gamma motor neuron discharge.
130.The BP recording of 2 males a hypertensive with reading of 200/110 and a normotensive with 120/80 was noted respectively. If 10mmHg is added to the mean BP of both how will the response of hypertensive patient vary from that of normal = Increase parasympathetic activity.
131.degree decrease in body temperature. What % age of CMRO ₂ decreases= 8%.
132.Preganglionic sympathetic fibers = White rami (14)
133.Parasympathetic activation causes =Increase secretions from various glands of body.
134.Parasympathetic loss affects which major component of body= GIT.
135.Cardiac muscles have sympathetic and parasympathetic these fibers are= Post ganglionic.
136.Lady accidentally cut radial artery which mechanism detects pressure= A beta.
137.Loss of water by evaporation and insensible loss from body = Depends on core body temperature.
138.Golgi tendon organ detects tension in which of following = Agonists.
139.Conduction in nerve fibers is slow down due to =Non – myelinated.
140.Parasympathetic stimulation causes= Bronchial constriction.
141.The action potential of a neuron = Is terminated by efflux of K ⁺ .
142.Cushing reflex triad (in Inc ICP) = Hypertension, bradycardia, Irregular respiration
143.When patellar tendon hit which of the following occurs =Quadrates femoris muscle contracts.
144.Man in marathon in July excessive sweating collapses cause =Heat exhaustion.
145.Inhibitory neurotransmitter is = GABA. Increase cerebral blood flow by= Halothane.
146.Which of these is not synthesized by post ganglionic sympathetic fibers= ACH (mainly they secrete NE)
147.Post ganglionic sympathetic fibers are present in = All spinal nerves.
148.Cerebral blood flow at rest = 50ml/100mg/min.
149.Upper and lower limits of cerebral blood flow autoregulation=50-150ml/min.
150.About sensation in periphery = Depending on modalities some pass while another bypass.
151.Neuron peak of action potential = Electric gradient tend to send K out of the cell.
152.Neurotransmitter released in chemical junction by = Ca influx
153.Regarding Axons = Carry impulses away from cell bodies.
154.True about alpha motor neuron= Myelinated. Preganglionic autonomic fibres are = B fibres.

155. Man waiting for the bus from in moderate hot environment. How body will regulate temperature = Hyperaemia.
156. Beta endorphins produced by = Hypothalamus.
157. Neuronal AP is due to = Influx of Na^+ .
158. Free nerve ending is = non-encapsulated receptor
159. At motor end plate, acetylcholine = Opens the acetylcholine gated ion channels which are linked to voltage gate.
160. Motor cerebral metabolic Rate for consumption of Oxygen is = 20 % of the total O_2 consumption at rest.
161. Adrenal medulla is supplied by = Cholinergic fibers.
162. Polysynaptic reflex = Cremasteric reflex.
163. Hot and burning sensation of heat stroke due to = Above 45 degrees.
164. Which of following lines the ventricles of brain and central canal of spinal cord = Ependymal cells.
165. Forceful stretching of muscle is done which of the following prevent muscles tear = Golgi tendon.
166. EEG of patient shows no A wave because patient is = Alert and conscious.
167. Norepinephrine is released by = Postganglionic sympathetic nerve fibres.
168. Young Medical student holding three books want to 4 th book from library upon holding the 4 th she drops all the books this is most likely due to = Inverse stretch reflex.
169. Neurotransmitter in slow wave sleep is = Serotonin. REM sleep related to (Med. Feb.) = Cholinergic (ACh)
170. After compensation of starvation which substance is used by brain = Ketone bodies.
171. Neurotransmitter in nigrostriatal pathway = Dopamine.
172. In a patient loss of proprioception occur after RTA what is underlying mechanism = Lateral Inhibition.
173. Steady pressure detected by which of following = Ruffini receptor.
174. True about pia matter is neuroanatomy = Extends into sulci and fissures of brain tissue.
175. Slow wave sleep is characterized by = Teeth grinding – NREM 2
176. Final common motor pathway is = Alpha motor neurons.
177. A patient came in emergency with hypoglycaemia coma what finding will be there = Sweating.
178. Temperature regulation is controlled by mainly = Anterior hypothalamus.
179. Sneeze reflex afferent = Trigeminal nerve
180. With exception of sweat glands parasympathetic system cause = Promote secretion.
181. Tactile two-point discrimination is done by = Meissner's corpuscles.
182. Semi-circular canal is for (Med. Feb.) = Angular acceleration.
183. Tears goes towards lacrimal sac via = Punctum and canaliculi.
184. Patient presented with peripheral tingling numbness and visual disturbance diagnosed what type of nervous system cells are affected in this disease = Oligodendrocytes.
185. Patients can't recognize the things object touching body with eyes closed lesion is at = DCML tract
186. Boy walking barefoot a pointed object pinches his planter surface he withdraws, receptors = Free nerve endings.
187. LP of normal patient done what will be findings of CSF to differentiate from plasma = Low chloride.
188. Heat loss from body depends on = Core body temperature.
189. Velocity of conduction increased 5-50-fold due to large diameter what will be other reason = Na channel permeability.
190. Parasympathetic activation cause = Relaxation of GIT sphincters
191. Opioids induce vomiting through which of following Alert and conscious = chemoreceptor trigger zone.
192. Posterior external arcuate fibers are other name for which of the following = Cuneo cerebellar tract.
193. Basal ganglia composed of = Striatum + globus pallidus + subthalamus + substantia nigra.
194. Knee reflex involve which of following = Muscle spindle.
195. Noxious stimulus is carried by = Lamina 1.
196. Dorsal column medial lemniscus link to thalamus via nucleus = Ventral posterolateral (VPL)
197. Ventral Spinothalamic carries which sensations = Tickling.
198. Raphe nucleus has which pain neurotransmitter = Serotonin.
199. Organophosphate poisoning causes = Pupil constriction.
200. During exercise max water loss by = Sweating. Supra optic nucleus release = ADH.
201. What lies posterior to cerebral aqueduct in midbrain = Tectum.
202. Medial lemniscus is formed by = Nucleus gracilis and cuneatus.
203. Left anterior Spinothalamic tract lesion because which affect = Right loss touch and pressure.
204. Patient can stand with eyes and has ataxia when asked to walk with close eyes ways back and forth where is the lesion present = Dorsal column.
205. A woman has loss of 2 points discrimination and fine touch in right leg. Which is defective = Fasciculus gracilis.
206. Amyotrophic lateral sclerosis affects = Motor system.

207. Which of following part of spinal cord affected in ALS = Ventral horn (motor).
208. Male had RTA with injury to occipital region now has homonymous hemianopia which is damaged = Optic radiation.
209. Most abundant cells in gray matter of CNS are = Protoplasmic astrocytes.
210. Sympathetic cholinergic stimulation cause which effect = Dilate blood vessel in skeletal muscles.
211. A person noticed some skin nodules ranging from 0.5 to 2mm in size there was a lesion in brain upon doing CT scan and some lesion in the abdomen was noticed with CT. What's the mutation involved in the disease = NF 1.
212. A patient having neck swelling with dropping of eyelids to diagnose condition which among these is suitable = Antibodies against acetylcholine receptors.
213. A patient presented with bilateral ptosis with muscle wasting on mastication suitable pathology is = Myasthenia
214. Feature that distinguishes partial transection of the spinal cord complete transection = Spinal shock.
215. Which of the following relay in substantia nigra = Pain.
216. Extradural Hematoma is caused due to rupture of which of the following vessel = middle meningeal artery.
217. Subdural hemorrhage is caused by damage to = Bridging veins.
218. Bell's phenomenon is = Eye globe moves upward when he tries to close his eyes.
219. Farmer with op poisoning feature = Bilateral pinpointed pupils.
220. Male with fluctuating type of deafness, on examination tympanic membrane retracted inward Rinne test is negative Weber lateralized to affected ear. What is the probable cause = Eustachian tube blockage.
221. Hearing improves in noisy environment in which of the following condition = Otosclerosis.
222. A stroke patient with irregular breathing related to = Cheyne Stokes breathing.
223. Patient having fever neck rigidity and slight SOB. CSF report reveals increase lymphocytes glucose 40 and proteins 400 what is likely diagnosis = TB meningitis.
224. A patient having temperature of 99°F cold clammy skin sweating profusely and working on a hot day brought to hospital in semiconscious state is most likely due to = Heat Exhaustion.
225. Patient with paroxysmal HTN & episodic headache is seen which of the following condition = Pheochromocytoma.
226. A patient presents with nerve deafness in one ear the test will show = High sound in normal ear.
227. Mechanism of action in fever is = increase prostaglandins.
228. After head injury a male presented with decreased thirst and low plasma osmolality. Cause of decreased thirst is = SIADH.
229. Brain tumor most commonly occur after radiation = Meningioma.
230. 2 nd Commonest brain tumor is = Meningioma.
231. Primary CNS tumour is = Glial cell tumour.
232. Hydrocephalus most common cause is = Aqueduct stenosis.
233. A man having high BP and decreased heart rate what is the cause = Raised intracranial pressure.
234. Loss of accommodation reflex lesion in which area = Cerebrum.
235. A male presented with severe headache and blurring of vision doctor performed the LP he found that the CSF is blood stained what could be the possible cause of blood-stained CSF cause is = Sub-arachnoid hemorrhage.
236. Old hypertensive man had thalamic hemorrhage the most prominent sensory finding system = Hyperesthesia.
237. The lesion occurred at the caudate and Globus pallidus of the brain. There was loss of GABA in substantia nigra the condition is of = Parkinsonism (prefer Dopamine loss – in exam the option was of GABA)
238. Parkinsonism affects which of these = Substantia Nigra.
239. A patient exhibiting hyperprolactinemia signs with decreased vision loss has a problem in = Pituitary.
240. Patient exhibits sign of myasthenia gravis what is best confirmatory test in him = EMG.
241. Damage in the nucleus of arcuate would result in = Kallmann syndrome.
242. The stroke due to berry aneurysm involves which artery = Anterior communicating artery.
243. The tumor of the posterior cranial fossa is = Medulloblastoma, Ependymoma, pilocytic astrocytoma
244. Brain tissues are damaged by stroke cell will be regenerated by = Astrocytes.
245. Cause of meningitis in newborn is = Streptococcus Lancefield B.
246. A female presents with balance problem exam Nystagmus in left lateral gaze a loss of the left corneal reflex and reduced hearing in the left ear. What is the most likely diagnosis = Acoustic neuroma.
247. Which ion is raised in malignant hyperthermia = Ca.
248. A security guard got gun-shot injury on lower back. After physiotherapy and rehabilitation, he had lost contralateral pain / temp below the level of lesion and ipsilateral loss of vibration what is diagnosis = Brown Sequard syndrome.
249. A young man presents with complaint of one-sided facial flushing and heat up with no sweating. Where is defect = Sympathetic loss. Supra optic nucleus lesion with loss of ADH will lead to = More loss of water in urine.
250. Child disturbed behavior suffering from fever and convergent squint. Which of following is most likely diagnosis = Tuberculosis meningitis.

251. Patient present with of dizziness and diplopia now presented with coma, cause = Basilar artery thrombosis.
252. Middle aged man presented with meningitis after having lung abscess cause is = Staph aureus.
253. Kid with meningitis then develops bilateral deafness due to = Damage to the neural pathways.
254. Damage to first lumbar vertebra will lead to = Conus Medullaris syndrome.
255. Post syphilitic patient can't constrict pupil on light with intact accommodation most suitable cause is = Argyll Robertson pupil.
256. A young girl finds it hard to hear at low frequencies = Conductive hearing loss
257. Dopamine and acetylcholine imbalance in corpus striatum leads to = Parkinson.
258. Only nerve affected in multiple sclerosis is = Optic.
259. Person is in prolonged coma which one involved = Periaqueductal.
260. Causative agent of meningitis in newborn = S. Agalactae.
261. Hypogonadism + anosmia lesion in = Arcuate nucleus.
262. Which one dec blood supply to brain = Hyperbaric O2.
263. Main reason for development of brain abscesses = Hematogenous spread of infection.
264. 6 months to 2yrs of age cause of meningitis is = S. Pneumonia.
265. Patient has intractable long history of pain and has taken various painkillers. How do you treat the patient then = Psychological cognitive treatment.
266. A patient presents with only complain of resting tremors area of brain involved = Substantia nigra.
267. Ocular manifestation in myasthenia gravis is due to = Decrease post synaptic ACH receptors.
268. A patient [resented with stroke in emergency his CXR shows Kerley B line. What is diagnosis = Intracranial bleeding.
269. 3 rd cranial nerve involves in = Brain herniation.
270. Verocay bodies resent in = Schwannoma.
271. A person presented to you with history of severe headache and vomiting at start of day. There was a tumor suspicion on radiography which was in cerebellar area involving granular layer what it can be = Medulloblastoma.
272. In post epileptic patient time taken from fits to normal state = Post ictal.
273. Interruption of cervical sympathetic chain result in Horner syndrome if Sympathetic nerves to the Eye are affected which one of the following is the commonest finding = absence of sweating on affected side.
274. Lady heard his husband saying that the neighbour loves her but do not confess which further proves his secret love. Which makes her sad. She is preoccupied with this thought sometimes get confused. The cause is = Delusion.
275. Alzheimer's diseases associated with which of following disease = Down syndrome.
276. Colleagues complain about a woman who forges signs on imp documents and search for belongings of others in their absence. Has joined another company and started smoking he has history of taking some drugs what test you would do for psychiatry evaluation = Urine analysis for drugs.
277. A patient after lesion of caudate putamen and loss of GABA neuron is suffering from which disease = Chorea.
278. Malignant hyperthermia receptors are = Ryanodine receptor.
279. A patient with color blindness can't differentiate between red from green this is called = Protanopia.
280. Patient after history of stroke develops brain necrosis, type of necrosis will be seen = Liquefactive necrosis.
281. 26-Year-old patient came in ophthalmology OPD with complain of inability to differentiate between different colours where is the pathology = Parafovea
282. old male with mask like facies, resting tremors, this is due to lesion in = Caudate lesion
283. old man presented in with unusual facial expressions, half side of the face was red and absence of sweating what could be the possible cause for this condition = Cervical Sympathetic Chain damage
284. male treated for meningitis, now came with morning headache having B/L papilledema cause is = Hydrocephalus
285. A patient feeling unwell from 3 days, anorexic headache, and neck stiffness. Lumbar puncture done which shows 100% lymphocytosis, low protein with glucose 84 what is disease = Meningitis
286. A mother delivered a child and brought her 5 days baby with fever, neck stiffness cause = Grp B streptococcus
287. Suspicion of pseudoseizure in = Absence seizure
288. A patient has presented with history of unconsciousness fits, high grade fever and dark coloured urine for one day CSF exam is unremarkable, diagnosis is = Cerebral malaria
289. In Alzheimer disease brain finding will be = Atrophy of brain
290. Petit mal epilepsy shows = Spike and slow appearance
291. Regarding pituitary gland true is = Inferiorly the adenoma compresses optic chiasma
292. A police man was sent to you because his urine has some opioid and other drugs, his response will be = Denial – it is the most common defensive mechanism.
293. Halothane causing malignant hyperthermia by = Continuous muscle contraction

294. Myasthenia gravis most initial test is = Tensilon test
295. Brain has ischemic stroke, most likely cause = Atherosclerosis
296. Child walks during sleep. This condition is called as = Somnambulism
297. Anterior pituitary removal led to = Absence of menses
298. Patient having 12 years of diabetes have decreased visual acuity. O/E it showed white spots and exudates on retina. Most likely due to = Central retinal vein occlusion
299. Myasthenia gravis bilateral ptosis, what test will be the test to diagnose = EMG > Acetylcholine receptor antibodies
300. A patient with Ptosis and Mydriasis likely due to damage = Oculomotor nerve
301. Stroke and brain tissue are damaged now repair is by = Astrocytes
302. After thoracolumbar outflow cut which one affected = Blood vessel
303. Sub Dural hemorrhage involves which vessel = Bridging veins > Superior cerebral vein
304. Patient having seizures due to decrease presynaptic reuptake of = GABA
305. HIV positive patient with fever from 4 to 5 days vomiting from 1 day CSF Glucose 80 BSR 110 CSF Protein 45 with no cell raised cause in HIV patient is = HSV Encephalopathy.
306. Most common cause of pale brain infarction = Atherosclerosis.
307. If basilar artery is blocked it will cause = Quadriplegia.
308. Common site of pyogenic brain abscess = Frontal lobe.
309. Meningitis in newborn cause by = Grp B Streptococcus > E Coli > Listeria
310. Gene amplification childhood tumor = Neuroblastoma.
311. EDH blood will accumulate = Between Dura and Calvaria.
312. Most radiosensitive brain tumor = Medulloblastoma > Brain stem glioma.
313. Organism responsible for causing meningitis HIV patient = Cryptococcus
314. A patient after CVA has loss of appetite to food and drink and tendency to throw because of his Decrease thirst is = stimulation of medial hypothalamus > SIADH.
315. Lesion at hippocampus result in = Loss of new memory.
316. Lucid interval present in = epidural hematoma.
317. Head injury biconvex hemorrhage vessel ruptured is = MMA.
318. Brain tumor immunohistopathology GFAP + tumor of which cells = Astrocytes.
319. Patient with Resting tremor stooped posture shuffling lesion in = Midbrain (Substantia Nigra)
320. Patient after being operated of brain tumor now presented with excessive appetite thirst. Which hypothalamic nucleus is damage = Medial.
321. Pituitary tumor invades which bone = Sphenoid body.
322. Prosopagnosia occurs due to lesion in = Inferior temporal lobe > Parieto-occipital-temporal lobe.
323. A person with empty speech area damage = Wernicke's.
324. Lateral hypothalamus injury result in = Inhibition of feeding (lateral lesion makes you lean)
325. Blow to temporal region cause involvement of which artery = Middle meningeal artery.
326. A person after RTA cannot speak lesion at which of following area = Broca area.
327. Progressive vision loss patient is due to slowly developing thrombi in which vessel = PCA.
328. If accommodation to remains intact and light reflex is absent where will be damage = Pretectal area.
329. H/O Viral infection in a person, he presents with vision loss and later Loss of accommodation reflex also, but light reflex is present = Encephalitis
330. Patient having Xerostomia likely nucleus involved = Superior Salivatory nucleus.
331. Right sided paralysis and loss of vibrations tongue deviated to left lesion in = Medulla.
332. Lesion in parietal lobe causes = Astereognosis (Somesthetic association area > Primary sensory area/cortex).
333. A man after RTA suffer injury to cervical sympathetic chain most likely change in eye = Ipsilateral pupil constriction.
334. A patient has gradual vision loss and laser photocoagulation was done which structure involved = Retina.
335. A patient having intention tremor he is having lesion in = Cerebellum.
336. Characteristic of cerebellar lesion = Dysidiadochokinesia.
337. Which type of loss occur due to lesion at postcentral gyrus = sensory area.
338. Pendular knee jerk is characteristic of following = Cerebellar lesion
339. A patient has damage to a nerve coming out from dorsal surface of left side of brain stem. What will be the defect in this patient = Left sided loss of intorsion.
340. In internal capsule injury what will be affected = Spastic paralysis of opposite side.
341. smoker and diabetic patient presented with partial ptosis small pupil and miosis diagnosis = Horner syndrome.

342.60 yrs old man presented in ops with unusual facial expressions half side of the face was red and absence of sweating what could be the possible cause for this condition = Cervical sympathetic chain damage.
343.A patient with ptosis and Mydriasis likely due to damage of = Oculomotor nerve.
344.A patient presented with paralysis of right limb and right lower face along with homonymous hemianopia lesion present is which pf of following = Forebrain.
345.Damage to cerebro-parietal area. What will be affected = Loss of tuning fork sensation.
346.A patient has problem of anosmia and hypogonadism, will be having lesion on MRI = Hypothalamus.
347.A patient present to you with both lower limb weakness, gait abnormality, and has peripheral tingling sensation he is more commonly have = Astrocytoma.
348.A young lady has aphasia due to lesion of non-dominant Broca's area lesion = Anomic aphasia.
349.Person who writes from his left hand he suffered an RTA and head injury ant differentiate from left from right and difficulty and word retrieval he has injury of = Right parietal. (Grestmann's syndrome)
350.A patient come with RTA and has spinal cord lesion completely cut what are the findings = Spastic paralysis.
351.54 yrs old, male went to doctor with complain of weakness of left half of body O/E he has tremors of left hand at and of movement. Muscular hypertonia of left limb and tendency to fall on left side. All cranial nerve intact neurological lesion located in = Left Cerebellar.
352.A patient comes to ophthalmology clinics with complain of gradual loss of vision his accommodation reflex was lost but light reflex was present = Presbyopia
353.Woman with peripheral tingling and numbness diplopia visual disturbances diagnosed as having a demyelinating disease which of the following would be affected = Oligodendrocytes.
354.Stab injury to neck posterolateral muscle is damaged, what will be affected =Turning of face (neck) to opposite site.
355.Old age patient complains of difficulty in reading near things and accommodation issue what is the cause = Lens curvature lost
356.A patient presented with Hemi-section of spinal cord at mid Hemi-section of what changes regarding upper motor neuron will be seen = Increased muscle tone and hyperreflexia ipsilaterally
357.A patient presented with hemisecting of spinal cord what change could be seen in the patient = Contralateral loss of pain & temperature below the lesion site.
358.After gunshot injury to lower back patient has loss of contralateral pain sensation but intact temperature sensation what is the likely diagnosis =Section of dorsal root SI.
359.Man with normal hearing but can't recognize the source from which sound is coming = Lateral Superior Olivary lesion
360.Bulbar palsy caused by = Motor neuron disease.
361.A newborn is brought with lumbosacral swelling containing meninges without neural tissue what is most likely diagnosis of this swelling = Spine bifida with Meningocele.
362.A patient sustained injury to posterior head and occipital lobe resulted in vision loss artery involved is neuroanatomy =Posterior Cerebral artery.
363.Which of following finding will be found in person having bradycardia and hypertension =Raised ICP.
364.A patient having paralysis of right side of body with deviation of angle of month of the left Dribbling of saliva patient can close both eyes. Injury at the level of = Supranuclear.
365.A patient having hemiplegia with same side deviation of angle of mouth and lateral rectus affected, lesion in =Pons.
366.Mass in premotor antero-inferior part of parietal lobe affected result in = Leg movement affected (ACA involved).
367.A female having postpartum hemorrhage during delivery of twins after that she can't lactate her babes, she also complains that she remains lethargic after delivery where is problem that she can't lactate =Sheehan syndrome
368.CSF examination necessary to rule out =Retinoblastoma / melanoma of eye.
369.in internal capsule hemorrhage following will be present = Contralateral UMN signs.
370.A patient having senseless speech and cannot remember which is said due to lesion of =Temporal lobe with mammillothalamic Tract.
371.In hydrocephalous which structure is most commonly blocked = Aqueduct of Sylvius.
372.Corticospinal tract myelination completed when= After birth.
373.After gunshot injury to spinal cord lesion at c7 following will happen =Contralateral loss of pain and temperature.
374.A patient has RTA he does not know recent event, but he remembers his school events, lesion of = Hippocampus.
375.Skilled and fine movement of distal limbs is controlled by = Cerebellum
376.Fine, skilled discrete movements carried out by = Corticospinal tract.
377.Patient has excruciation right leg pain anterolateral right leg chordotomy was performed which tract was involved= left lateral Spinothalamic tract.
378.Patient after RTA having sacral region of spinal cord damage has which effect = Autonomous bladder.

379. Proximal muscles tone depends upon which tract = Rubrospinal tract.
380. Medial lemniscus is formed by = Nucleus gracillus + cuneatus
381. After severe trauma to spinal cord patient having loss of all sensation bilaterally due to = Complete cord transection.
382. Tabes dorsalis cause which of following = Atonic bladder.
383. A child with a mass at lumbar region, it has meninges without neural tissue. It is = Spinal bifida with Meningocele.
384. Patient presented with inability to write read and understand most likely lesion is in = Wernicke area.
385. There was Hemisection of vertebra what will be lost contralateral = Warmth / temp.
386. Nucleus pulposus will be seen herniating at which segment = L4- L5 > L2-L3.
387. patient after post thyroidectomy developed hoarseness of voice examination reveals sluggish movement of vocal cords nerve damage related to which area = CNX.
388. A female with sign and symptoms of hyperprolactinemia was diagnosed with pituitary adenoma. The growth of this tumor anteriorly will compress which structure = Optic nerve.
389. A patient came with blow to antero inferior part of temporal region and period of unconscious for 3 mins and vision problem most likely vessel damage = Anterior division of MMA.
390. Cephalohematoma occur commonly at which of following location = Between skull and periosteum.
391. After gunshot injury to lower back patient has loss of contralateral pain sensation but intact temperature sensation what is the likely diagnosis = section of dorsal root S1.
392. Post rotatory nystagmus is caused by = Endolymph in semi-circular canals.
393. Cat is denervated at mid collicular level what will happen = Decerebrate rigidity.
394. Climbing fibers to purkinji arises from = Inferior olivary nucleus.
395. Middle meningeal artery branch of = Maxillary artery.
396. Patient has lost fine touch vibration and proprioception in lower limbs where is the lesion = Nucleus gracillus. Nucleus gracillus lies medially, while nucleus cuneatus lies laterally in spinal cord.
397. Ligament pierce at last during epidural is = Ligamentum flavum.
398. On histology show flask shaped cells multiple dendritic synapses in = Cerebellar cortex
399. Patient head is turned to see nearby object which part of brain involves = superior colliculus.
400. Structure connects hippocampus and hypothalamus is = Fornix.
401. 2 nd order neurons of anterior Spinothalamic tract lie in = Substantia gelatinosa.
402. Critical tactile Sensation carried by = Posterior white Colm
403. Patient with right sided hemiplegia, left sided pain and temp lost below T8 while right proprioception and touch sensation lost below T8. What is the cause = Hemi section at T8
404. Pain, temperature & crude touch from face is carried by which of following tract = Trigeminothalamic
405. Corpus striatum contain = Caudate + Lentiform
406. Higher intellectual function of brain by which part = Wernicke's area.
407. A patient had RTA; he does not know recent event, but he remembers his school events which lobe is involved in amnesia = Temporal lobe.
408. Cingulate gyrus is supplied by which of following = Anterior cerebral artery.
409. Corpus callosum contains which fibers = Commissural fibers.
410. What is the primary function of basal ganglia = Planning voluntary control.
411. A patient with enlarged hand and feet with associated joint on MRI mass compressing optic chiasma was found what can occur in this patient = Bitemporal hemianopia.
412. Dorsomedial nucleus of thalamus related with of following = Fear and fright memory.
413. Lateral to medial arrangement of cerebellar nuclei is = Dentate, Globose, and fastigial.
414. Lower limb proprioception carried by gracillus in spinal it is located = Medial.
415. Connection of amygdala and hippocampus = Mammillothalamic body.
416. During sympathectomy which lumbar ganglion is spared = L1.
417. Patient in depression lack of motivation due to lesion in = Frontal lobe.
418. A patient's blindfolded asks to identify the structure in hand which area assessment is being done = Somesthetic association area.
419. A patient presented with right side hemiplegia without sensory loss lesion is at which site = Left internal capsule.
420. Posterior external actuate fibers Related to which of following = Cuneo cerebellar tract.
421. A 65 yrs. male develops right sided hemiplegia and slight deviation of angle of mouth of left while talking he can close his eyes on command what other finding can be present = Clasp knife spasticity.
422. Fluent nonsense speech is due to damage of which area = Wernicke's area.
423. Lesion of geniculocalcarine tract cause which defect = Homonymous hemianopia with macular sparing.

424. Lesion at right optic tract result in blindness = left homonymous hemianopia.
425. Point by point discrete movement of painter carried out by which tract = Corticospinal tract.
426. Sign of sensory speech area damage = Fast speech that make no sense.
427. Right frontal lobe optic tract compressed leads to = Left homonymous hemianopia.
428. After RTA patient suffered change of behaviour and decrease motivation due to lesion in which of these = Frontal lobe.
429. Patient after RTA sacral region of spinal cord damage has which effect = Neurogenic bladder.
430. A patient after RTA having precentral gyrus lesion affect will be = Right hemiplegia.
431. Injury to pyramid function loss will be = Motor loss.
432. A section of caudal pons consists of horizontal fiber. These fibers are of = inferior cerebellar peduncle.
433. A patient having atrophy of the calf muscles and loss of reflexes with weakness of legs the lesion in = LMN lesion.
434. Acute memory loss due to which area damage = Limbic association cortex.
435. Acoustic area location is = Superior temporal.
436. Brodmann area 3,2,1 = Receive all somatosensory sensation
437. Structure buried in lateral sulcus of cerebrum is = Insula (Left insula → Feeling of disgust, supplied by MCA)
438. A patient presented with neck rigidity fever and altered state of conscious, for lumbar puncture which of the following is ideal site = Above the spinous process of L4.
439. Why association of nausea and vomiting with vertigo = Close interaction of vestibular and vagal nuclei
440. Characteristic of cerebellar neoplasm = Ataxia.
441. Babinski sign is due to damage in which of following area = Pyramids.
442. In lesion distal optic chiasma on left side the visual defects will = Right homonymous hemianopia.
443. Which type of loss occur due to lesion at postcentral gyrus = Sensory area.
444. Person after RTA is unable to speak and has non fluent speech but can understand commands lesion is in which of following = Broca's area.
445. Subarachnoid space = Between arachnoid and pia mater.
446. Feeding centre location in which of following = Lateral nucleus of hypothalamus.
447. Which structure lie closest to crus cerebri = Substantia nigra.
448. Nucleus tractus solitaries contain which of following = Body of 2 nd order neuron of taste pathway.
449. Perception of disgust by which area = Left insular cortex.
450. Which sensation is carried through the dorsomedial nucleus of thalamus = Fear and anxiety.
451. Patient eyes looks towards the site of lesion horizontal gaze center has lesion in = frontal eye field.
452. Patient with right sided hemiplegia and facial palsy of left of the face lesion in which of following = Pons.
453. Old male hypertensive presented in the emergency with left side hemiplegia and bilateral pinpoint pupils lesions seen in = Pons.
454. Myelination is the peripheral nervous system is formed by = Schwann cells.
455. Before voluntary movement the image is formed in which area of brain = Anterior part of premotor area.
456. A child born with a mass at lumbar region with no neural tissue in it = Spinal bifida with Meningocele.
457. Person with pituitary adenoma having bitemporal heteronymous hemianopia lesion lies at = Optic chiasma.
458. Ligament pierce to reach epidural space = Ligamentous flavum.
459. Wernicke area located in = Superior temporal gyrus.
460. Lesion in basal ganglia causes = Involuntary movements.
461. A patient with loss of accommodation and 3 rd Nerve palsy where is lesion = Midbrain.
462. Pathway to recognize object on hand or foot without visual stimulus = Dorsal column medial lemniscus.
463. A person after having RTA complains of leg weakness and difficulty to walk which artery of brain is likely involved = ACA
464. Projecting fibers are found in = Internal capsule.
465. What is normal CSF pressure = 10 to 25 cm of water
466. Continues capillaries present in = Brain.
467. After RTA patient suffering from bitemporal heteronymous hemianopia lesion in = Middle part of optic chiasma.
468. Regarding max determinant of CSF composition = Ependymal cells.
469. Antigravity muscles are maintained by = Vestibulospinal.
470. Hemiballismus is due to lesion in = Sub thalamus.
471. Main blood vessel location is = Subarachnoid space.
472. Site of lumbar puncture = L4/L5
473. A patient having cerebral trauma after that decreased appetite and thirst cause is damage of = Lateral hypothalamus.
474. Increase neuronal activity before a skilled voluntary movement = Cortical association area.

475. Dysphagia dysarthria ipsilateral Horner, ipsilateral face sensation lost artery involved = PICA.
476. Right sided upper and lower limb paralysis and tongue deviated artery involve= ASA.
477. Interlaminar space is used for delivery of injection into = Epidural.
478. Cerebellum is connected to the midbrain through= Superior cerebellar peduncle.
479. Fibers of upper motor neurons are decussated in = Medulla.
480. Cerebral aqueduct of Sylvius present in = With in brain stem
481. Herniation between L4 and L5 affects which spinal segment = L5
482. Middle cerebellar peduncle contains which tract = Pontocerebellar.
483. Hippocampal injury cause = No new memory. Proximal flexor muscles controlled by = Rubrospinal.
484. The structure most likely pierced by the needle during lumbar puncture is = Ligamentum flavum.
485. Pain inhibitory system in brain spinal cord located in which of following = Raphe magnus nucleus.
486. Left pons connection with = Right cerebellum left cerebrum.
487. Corticospinal tract decussates at = Pyramid. Damage to dorsal column tract cause = Sensory ataxia.
488. Subarachnoid space in adults ends at = S2.
489. Tractus solitarius is formed by cell bodies of = Second order neurons of taste fibers.
490. Left temporal gyrus/lobe lesion results in = right superior quadrantanopia.
491. L5 displace forward on S1 in which disease = Spondylolisthesis.
492. Adjacent spinous processes of sacrum fuse to form= Median sacral crest.
493. Patient is having restricted movement in left lateral gaze inability to close left eyes and loss of hearing of left side site of lesion= Cerebello pontine angle.
494. Part of temporal lobe visible in medial surface of hemisphere = Inferior temporal lobe.
495. Slow writhing movement are called athetosis due to defect in which of following= Globus pallidus.
496. Right optic tract lesion cause vision loss = Right nasal and left temporal.
497. Thalamus blood supply is by = PCA.
498. Right side hemiplegia and right-side facial palsy (angle deviate to opposite) lesion most likely in = Cortex.
499. Patient with right hemiplegia double vision on seeing side lesion of = Midbrain.
500. Arachnoid + pia merge to form coccygeal ligament at which level = S2.
501. CT of patient shows dilatation of right lateral ventricle. Most likely blockade = Foramen of Monro.
502. Cajal stain cells within CNS with multiple cytoplasmic processes= protoplasmic astrocytes.
503. Reticular formation location = Floor of sylvian Aqueduct.
504. Woman presented with bitemporal hemianopia & inverse prolactin level = Pituitary Gland.
505. Slow component of nystagmus is controlled by = Vestibular apparatus.
506. Broca's aphasia due to blockage of = MCA.
507. Olfactory nerve cells repair or change in every 2 weeks = Basal cells.
508. Pt came with dysphagia polyuria & sleeping disorders lesion in = Hypothalamus.
509. Retired officer came with c/o tremors while doing small work! Gait asked to touch nose, lesion in = Cerebellum.
510. A man with presented stroke ACA is affected It will affect which area of brain= Somatosensory area.
511. Most of the optic fibers ends at = Lateral geniculate.
512. Regarding weber syndrome= Contralateral paralysis with ipsilateral ptosis and lateral deviation of eye.
513. Clark nucleus level = C8- L2.
514. Nucleus ambiguus contains= CN 9,10,11.
515. Dorsomedial nucleus of thalamus related with= Memory.
516. Which of the following is trigeminal reflex= Corneal reflex.
517. Prosopagnosia mean= Inability to recognize faces.
518. Medial part of frontal & parietal lobe blood supply = ACA. Nucleus pulposus derived from= Notochord.
519. Related to lateral corticospinal tract = Rubrospinal
520. loss of pain & temperature sensation but intact touch sensation in which of the following= Syringomyelia.
521. Cranial neuropore closure defect with absent brain caldarium = Anencephaly.
522. Patient with upper motor neuron lesion exhibits signs of right-side hypertonia with exaggerated reflexes & positive Babinski's sign which of the following are affected = Left Brodmann area 4.
523. Highest presentation on the motor homunculus= Hand / thumb.
524. Injury at foramen Ovale will lead to = Loss of sensation of at lower face.
525. Xerostomia dry eyes & otitis media where id the nuclei located=Pons
526. Circle of Willis is formed by = 2 Vertebral + 2 ICA

527.Face sensation lost along with hearing loss which of the following is the site of lesion= Internal auditory meatus.
528.Which of the following is the nucleus of central medulla= Nucleus ambiguus.
529.Spinal nerve comprises of which of the following= Motor & sensory component.
530.Which of the following is correct route of CSF route = Foramen magnum to subarachnoid space.
531.Vagus nerve cut & central part stimulated will lead to = Apnea.
532.A patient has ataxic gait & ipsilateral face sensation lost where is the site of lesion= Cerebellopontine angle.
533.Accommodation reflex intact but light reflex is lost due to lesion in = Pretectum.
534.A patient presents with stroke which has result in left sided hemiplegia and he is unable to talk (aphasia), this lesion is because of which affected artery= MCA.
535.Rathke's pouch is the derivation of = Stomodaeum.
536.A patient presents with unique choreiform movements due to the lesion to= Caudate
537.The process of long-term memory involves=Protein synthesis.
538.Babinski sign is positive in lesion in which of following =Pyramidal lesion.
539.The part of the brain responsible for anxiety emotions and rage=Amygdala.
540.The lesion in left pre-central gyrus would result in =Right sided hemiplegia.
541.Nerve supply of the adrenal medulla is = Greater splanchnic nerve.
542.A patient having paralysis of right side of body with deviation of angle of mouth to the left and dribbling of saliva, but the patient can close both eyes. Injury is at the level of = Supranuclear.
543.Sensory supply to the eyes is lost and the jaw movements are intact. Which of the following has undergone lesion = Sensory nucleus of trigeminal nerve.
544.Damage to the cranial nerve IX (9) the taste sensation lost would be=Bitter.
545.The brain structure embedded in lateral hemisphere= Insula.
546.The calcarine sulcus is involved in which sensations= Visual.
547.Spinal cord supplied by which of the following= Spinal artery.
548.Vertebrae limited by = Anterior & posterior longitudinal ligaments.
549.Regarding corpus callosum true s = most fibers interconnect symmetrical areas of cerebral cortex.
550.True about motor cortex, present in = Frontal lobe.
551.Cortical area with maximum representation on sensory homunculus = Lips.
552.Spinal anaesthesia is given in=subarachnoid space.
553.Which space is assessed after piercing the inter laminar ligament during LP=Epidural space.
554. right sided weakness and loss of vibration sense and tongue deviated to left lesion was= Middle of medulla.
555.Septum pellucidum is bounded superiorly by = body of corpus callosum.
556.A man had gunshot wound to the spine after which he lost sensations to lower limbs loss of power but increased tone and up going plantar with central clonus lesion at = Both corticospinal and lateral Spinothalamic.
557.What is age of closure of anterior fontanelle= 24 Months.
558.Cephalohematoma most common site is = Under periosteum.
559.Weakness of right of body and diplopia on looking left = Midbrain.
560.Superolateral relation of floor of 4 th ventricle=Superior cerebellar peduncle.
561.Person has problem with reading writing and speaking lesion in = Left frontal and temporal.
562.Lucid interval after injury then again loss of consciousness= Epidural hematoma.
563.Sacral hiatus= Unfused S4 and S5.
564.Microglial cells= Macrophages of CNS.
565.Labyrinth artery sometimes is a branch of = AICA.
566.Fibers after decussating in medulla are called= pyramidal fibers
567.Medial geniculate body a thalamic nucleus= Lies on the mid brain.
568.Lesion at right precentral gyrus cause= Exaggerated knee jerk on left.
569.If thalamus gets damage which is not affected = Sense of Olfaction.
570.Dorsal nucleus of vagus nerve is = Medulla.
571.Posterior communication artery = Passes above the oculomotor nerve and connects ICA and PCA.
572.Internal carotid artery = At bifurcation its lateral to external carotid artery then turns medially and posteriorly.
573.Primary brain vesicle= Mesencephalon.
574.PICA damage blood supply of which part will be affected= Dorsolateral of medulla.
575.Regarding brainstem reticular formation= Unusual stimulus causes arousal.
576.How many white ramus communicants are there in our body = 14.
577.Basal ganglia send excitatory signals to= Thalamus + Motor cortex

578. In CSF Proteins = 20-40 mg/dl.
579. Spinal cord supported by = Denticulate ligament.
580. Nerve growth rate in the case of peripheral nerve damage = 1-3 mm/d
581. Brain venous drainage = Dural venous sinuses.
582. Optic chiasma damage with also hypothalamus damage result in = Hyperphagia.
583. About cerebellum true is = Lies below tentorium cerebelli.
584. Which part of brain receives major excitatory input to from cerebral cortex = substantia Nigra.
585. Posterosuperior relation of pituitary = Sphenoid air cells.
586. Coccygeal segment of spinal cord lies at the level of = L1.
587. Thoracolumbar outflow composed of = sympathetic.
588. Basic electrical rhythm of brain is location in = Reticular formation.
589. Rexed lamina 3,4 presents in = Posterior gray horn.
590. Most abundant sphingolipids in gray matter of the brain = Sphingomyelin.
591. Parasympathetic flow to heart via = Vagus nerve.
592. Ventral Spinothalamic tract carry = Itch and tickle and present till Mid-thoracic region
593. Parasympathetic origin in spinal cord = S2 S3 S4
594. Left half of pons is related to = right cortical tract & Left olivary nucleus.
595. Anterior & posterior spinal arteries are the branches of = Vertebral arteries and PICA respectively.
596. When a person encounters an obnoxious stimulus, he reflexively withdraws his limbs & body away from the stimulus most appropriate Statement regarding this reflex is = Remains for many months after complete Transaction of cord
597. Dorsal column fibers of lower body related to upper body at cervical level = Medial to lateral.
598. Death is caused by bilateral damage to which nerve = Vagus.
599. Cervical segment of spinal cord does not have = Lateral horn. What is not present at L4 = Lateral horn.
600. Synapses absent in = Dorsal root ganglion.
601. Basal ganglia damage will not cause = Intention tremors.
602. Inferiorly the floor of fourth ventricle has medially which structure = Hippocampus.
603. Which stimuli will produce minimal neurologic activity in thalamus = Olfactory.
604. Two kids bet eye blinking the one kid lost as he blinked 1 st this blinking was sue to = Cervical segment of spinal cord (Superior cervical ganglion).
605. Medial lemniscus formed by decussation of = Internal arcuate fibers DCMC.
606. Superior colliculus is compressed it will affect eye cause what = Contralateral saccades, effects horizontal movement.
607. All central Primary somatosensory Nucleus were damage. Which ones of these are primary sensory = Dorsal grey of spinal cord + dorsal white column + trigeminal nucleus. (All of these are 1° sensory).
608. In RTA loss of phonation and can't speak which area damage = Posterolateral part of inferior frontal gyrus.
609. Visual fibers after crossing chiasma passed = Lateral geniculate body to optical radiation
610. Optic nerve is = SSA.
611. After gunshot injury at L1 a man presented to you with loss of pain and temperature on right side. Where is the lesion = Left lateral Spinothalamic tract.
612. Major blood vessels in brain in present in = Sub arachnoid.
613. Part of brain involved in intelligence = frontal lobe.
614. Lesion of geniculocalcarine tract cause = Homonymous with macular sparing.
615. Which one directly control autonomic reflex system of body = Hypothalamus.
616. Neuroepithelia of nose is = Bipolar.
617. A man unable to hold a mug of coffee an image drawn of shoulder and hand movement on = Premotor area.
618. Agranular cerebral cortex is present is = Primary motor area.
619. Neo striatum contains = Caudate + putamen.
620. Hyphaemia is = Blood in anterior chamber.
621. Child presented with scaphocephaly which suture closed prematurely = Sagittal.
622. Furunculosis on tip of nose spreads to cavernous sinuses via = superior ophthalmic vein.

MICROBIOLOGY

BACTERIOLOGY

- Bacteria: microorganisms having Prokaryotic cells lacking definite Nucleus.
- Mesosomes are organelles present in bacteria for respiration.
- Ribosomes are 30S, 50S, 70S total.
- Bacteria are beneficial and can cause diseases as well.
- Bacteria divide by Binary Fission (asexual reproduction)
- DNA is circular / Linear.
- Plasmid is small Circular, double stranded DNA independent of chromosomes.
- Transposons are Jumping genes which can copy and excise itself and insert into same DNA molecule or unrelated DNA. This process is called transposition. it creates multiple drug resistant Plasmids.

Growth phase is divided into 4 phases as: Lag phase, Log phase, Stationary phase, and death phase.

1. **Lag phase:** Period of no growth
2. **Log phase:** Period of Exponential growth. Rapid inc in No. of bacteria (antibiotics effect the LOG phase)
3. **Stationary phase:** Rate of cell division is equal to cell death
4. **Decline/Death phase:** Rate of cell death is greater than cell division.

TRANSFER OF GENETIC MATERIAL B/W BACTERIA

<u>CONJUGATION</u>	<u>TRANSDUCTION</u>	<u>TRANSFORMATION</u>
<ul style="list-style-type: none"> • Direct transfer of Plasmid DNA between two bacteria using Sex pilus. • Requires physical contact b/w two bacteria. Only Plasmid and transposons can be transferred. • Resistant to DNase because DNA is inside bacteria. • E. coli can reproduce by conjugation. • No chromosomal DNA is transferred by conjugation 	<ul style="list-style-type: none"> • Transfer of DNA from one bacterium to another using Virus / Bacteriophage • Virus capable of infecting Both donor and recipient bacteria • Resistant to DNase. • Transduction may Generalized (via lytic phage) or Specialized (via Lysogenic phage). • Genes of Botox toxin, Cholera, Diphtheria, Shiga toxin and erythrogenic toxin of Group A strep are encoded in Lysogenic phage. 	<ul style="list-style-type: none"> • Uptake of extracellular Free or naked DNA from surroundings • Any DNA fragment i.e., Linear Chromosomal DNA or plasmid can be transferred. • Sensitive to DNase • Transformation is seen in: <ul style="list-style-type: none"> ✚ Strep pneumoniae ✚ H. influenza

EXOTOXIN

- Polypeptide secreted from certain spp of Gram +ve & Gram -ve bacteria, having high toxicity (high Fatal Dose) and various modes of actions with different clinical effects, inducing High titre antibodies called Antitoxins,
- Hence, can be Used as Vaccine and it is also rapidly destroyed at 60°
- Genes are located on Plasmid or bacteriophage.
- Examples: Botulism, cholera diphtheria, tetanus

ENDOTOXIN

- Lipid A component of Lipopolysaccharide of Gram-ve bacteria only that is released when cell is lysed (not secreted from cell), having low toxicity, induces;
- TNF, IL-1 & IL-6; causing Fever, Shock & DIC.
- Due to poor antigenicity, No. toxoids formed / vaccine available and it is stable even at 100°C for 1 hr.
- Genes are located on Bacterial Chromosomes
- Examples: Meningococcal sepsis

IMPORTANT FACTS REGARDING TOXINS AND PAST PAPERS BCQs

- ✓ Gram +ve bacteria are Most common cause of Septic Shock Overall.
 - ✓ SEPTIC Shock is Mediated or initiated by Cytokines action
 - ✓ Endotoxin activates: TNF alpha > IL – 1 activation
 - ✓ In Septic/ endotoxic shock 1st mediator released is TNF > IL-1
 - ✓ Last mediator to be released in septic shock is IL – 6
 - ✓ Endotoxin causes complement activation
-
- Pseudomonas uses Exotoxin A > endotoxin. Endotoxin for fever, hypotension and DIC.
 - Enterotoxigenic E. coli has Heat stable toxin (over activates cGMP) and Heat Labile toxin (which over activates cAMP)
 - Cholera Toxin over activates cAMP, permanently activating Gs (G stimulatory) increasing secretion of Neutral NaCl > Inc Chloride secretion from gut
 - Anthrax toxin mimics cAMP. Clostridium Difficile uses Toxin A & B.
 - Pertussis toxin inactivates Gi (inhibitory G) causing activation of cAMP.
 - Tetanus and Botox toxin are proteases that cleave SNARE protein used in NMJ transmission
 - Tetanus toxin is EXOTOXIN > NEUROTOXIN prevents release of inhibitory GABA+GLYCINE from Renshaw cells of spinal cord. Affects Motor Nerves
 - Clostridium Perfringens has Alpha Toxin which is Lecithenase. Double Zone of hemolysis.
 - Toxic shock syndrome Toxin: 75% of cases isolated from Staph Aureus. it is a Superantigen
 - Diphtheria toxin inactivates EF-2, inhibiting Protein synthesis.
 - TNF is produced 1st followed by IL1, NO etc.
 - IL1 > IL-6 induce Fever
 - TNF induces Fever +Hypotension.
 - Fever in pseudomonas sepsis / infection is due to TNF action
 - Overall, for Fever IL1 > TNF
 - IL-6 is the last mediator to be produced.
 - Endotoxin causes/ induces Complement activation.
 - Urinary tract is common source for Gram -ve Sepsis.
 - Streptolysin O contributes to Beta Hemolysis. ASO titres helpful in diagnosing ARF
 - Shigella toxin causes mucosal invasion whereas EHEC doesn't invade Host cells
 - Haemolytic uremic syndrome: Enterohemorrhagic E coli EHEC O157: H7 is involved

CLASSIFICATION OF BACTERIA

1. Based on Staining: Gram +ve, gram -ve and acid fast etc.
2. Based on Morphology / shape: Cocci, bacillus, branching / curved etc
3. Based on O2 requirements: Aerobes, Anaerobes and facultative etc.

GRAM STAINING

- Bacteria which retain Primary Dye due to thick Peptidoglycan layer in cell wall are called Gram+ve. They appear **Purple**
- Gram-ve bacteria retain **Sufranin** / 2ndry dye. They appear **Red**
- Some bacteria are not gram stained as follows. Mnemonics; **The Real Microbes Lack Color**.
- Treponema Palladium, Rickettsia, Mycoplasma, Legionella, Chlamydia

Primary stain	Crystal Violet
Mordant	Mordant/Fixes Dye: Iodine
Decolorizer	Alcohol / acetone
Counter stain or secondary stain	Sufranin (Red color)

CHARACTERISTICS	GRAM +VE	GRAM -VE
○ Peptidoglycan	Thick / multi layered	Thin
○ Teichoic Acid	Present	Absent
○ Outer Membrane	Absent	Present
○ Periplasmic Space	Absent	Present, having Beta lactamase
○ Toxin	Exotoxins only	Both Endotoxin and exotoxin
○ Lipopolysaccharide Content	None	High LPS


























	Obligate Aerobes	Facultative Anaerobes	Microaerophilic	Obligate Anaerobes
Gram + Ve	<ul style="list-style-type: none"> Nocardia – Weakly Acid Fast Bacillus Cereus 	<ul style="list-style-type: none"> Staphylococcus Bacillus Anthrax Corynebacterium Listeria Actinomyces 	<ul style="list-style-type: none"> Streptococcus 	<ul style="list-style-type: none"> Clostridium
Gram – Ve	<ul style="list-style-type: none"> Neisseria Pseudomonas Bordetella Legionella Brucella 	<ul style="list-style-type: none"> Most Gram -Ve Rods 	<ul style="list-style-type: none"> Spirochetes Treponema Borrelia Leptospira Campylobacter 	<ul style="list-style-type: none"> Bacteroides
Acid Fast	<ul style="list-style-type: none"> Mycobacterium Nocardia 	--		--
No Cell Wall	--	<ul style="list-style-type: none"> Mycoplasma 		--

MORPHOLOGY	GRAM + VE	GRAM – VE
Circular (Coccus)	Staphylococci, Streptococci	Neisseria
Rod (Bacillus)	Corynebacterium Listeria Bacillus Clostridium Mycobacterium (acid fast)	E coli, klebsiella, Enterobacter Salmonella, Shigella, Proteus Yersinia, Serratia Vibrio, campylobacter, helicobacter Bacteroides (anaerobic) Haemophilus Bordetella, legionella, brucella Francisella, Pasteurella, gardinalia
Spiral	--	Treponema, Borrelia, Leptospira
Branching Filaments	Actinomyces (anaerobes) Nocardia (weak acid fast)	--
Pleomorphic	--	Chlamydia, rickettsia
No Cell Wall	Mycoplasma	

GRAM +VE COCCI

- ✓ Staphylococci (in clusters) & streptococci (in chains) are 2 main species.
- ✓ These two are differentiated on the basis of Catalase Test only
- ✓ Staphylococcus spp are catalase +ve whereas Streptococci spp. are Catalase -ve
- ✓ Staphylococcus aureus is differentiated from other staphylococci based on COAGULASE test.
- ✓ Staph Aureus is both Catalase +ve & Coagulase +ve while rest spp of staphylococci are Catalase +ve but Coagulase -ve

STAPHYLOCOCCI		
Staphylococcus Aureus	Characteristics	<ul style="list-style-type: none"> Colonizes NOSE, Encapsulated Catalase +ve, Coagulase +ve Beta hemolytic. Mannitol fermenter--Forms Golden yellow colonies Resistant to multiple drugs Most common cause of Acute Osteomyelitis + Septic arthritis & Right sided Endocarditis (in IVDA) 2nd Common cause of Conjunctivitis Causes Lung Abscess and meningitis secondary to Lung Abscess. Or Lung abscess secondary to Meningitis Treat with Cloxacillin, while MRSA by Vancomycin
	Virulent Factors/Toxins	<ul style="list-style-type: none"> Protein A: most imp virulent factor that is Anti phagocytic -- Binds Fc of IgG Coagulase. 2nd imp one Toxic shock syndrome toxin -1 (TSST-1) Enterotoxin, PV Leukocidin, DNA-ases, Beta lactamase, Proteinases/Lipases, Exfoliating A, B, Capsule Resistance to Penicillin by transduction of Plasmid.
	Diseases	<ul style="list-style-type: none"> ❖ Food poisoning -- Diarrhea & Vomiting, immediately after 2- 6 hrs of meal caused by Enterotoxin. ❖ Toxic Shock Syndrome in Females Using tampons during menstruation. Presents with fever, Vomiting & shock. Caused by TSST-1 (super antigen) or Enterotoxin. ❖ Scalded Skin Syndrome Caused by exfoliation toxin A ❖ Most common cause of Localized skin infections. e.g., Abscess, furuncle, Carbuncles and Parotid crypt abscess ❖ Leading cause of Hospital Acquired infections. ❖ Most common cause of Wound infection
MRSA	Methicillin Resistant Staphylococcus Aureus/ MRSA <ul style="list-style-type: none"> Present in 20-40% People in anterior nares. Community acquired MRSA produces Panton-Valentine Leukocidin causing apoptosis of Neutrophils. If community Acquired MRSA: Give Vancomycin > septran > "Fusidic Acid If NOT, Community Acquired: Use Fusidic Acid Vancomycin is not given to all contacts 	
Staphylococcus Epidermids	<ul style="list-style-type: none"> Present on SKIN, Catalase + ve and Coagulase -ve. Also, Urease +ve Virulent factors include various enzymes, extracellular proteins i.e., adhesins. May cause infections related to Prosthetic devices /implants e.g., Hip implant and Prosthetic Heart Valves infection 	
Staphylococcus Saprophyticus	<ul style="list-style-type: none"> Catalase+ and coagulase -ve. Produces factors similar to other Staph spp. 2nd common cause of UTI Especially in Young Females (E coli is most common cause) 	

STREPTOCOCCI		
Streptococcus Pyogenes Or Group A Streptococcus	Characteristics	 Beta hemolytic, catalase -ve and Bacitracin sensitive
	Virulent Factors/Toxins	 M protein  Streptolysin O (ASO titres 1: 80 helpful in diagnosing ARF)  DNase, Erythrogenic toxin
	Diseases	 Scarlet fever (Erythrogenic toxin)  Pyogenic (Cellulitis), impetigo, pharyngitis  Rheumatic fever + glomerulonephritis  Toxic shock syndrome (Pyrogenic Exotoxin B)  M protein plays role in ARF & glomerulonephritis due to Similarity with myosin or Tropomyosin
	Diagnosis	 Throat Swab for pharyngitis -- gold standard.  Blood Culture or Latex agglutination test via antigen detection
	Treatment	 Amoxicillin / Augmentin / Macrolides e.g., Erythromycin
Streptococcus Agalactiae Or Group B Streptococci	❖ Beta hemolytic, colonizes Vagina. ❖ Capsule is virulent factor. ❖ Most common cause of Neonatal Sepsis, neonatal meningitis, and Puerperal sepsis	
Streptococcus Viridians	❖ Normal flora of Oropharynx, Alpha hemolytic and Optochin resistant . ❖ Most common cause of Bacterial endocarditis. ❖ <i>S. Mutans</i> > <i>Mitins</i> cause dental plaques. ❖ <i>Strep. Sanguinis</i> may cause Subacute Endocarditis	
Streptococcus Bovis	❖ Normal flora of GIT ❖ Always suspect Colorectal cancer when you find a case of <i>S. Bovis</i> endocarditis	
Enterococci	❖ Diplococci. Normal colonic flora ❖ May cause Endocarditis following GI / GU procedures, UTI, and biliary tree infections.	
Streptococcus Pneumoniae or Pneumococcus	Characteristics	 Alpha hemolytic, Optochin sensitive  lancet shaped Diplococci  Encapsulated, has IgA protease.
	Virulent Factors/Toxins	 NO Virulence without capsule  (Capsule is the most potent virulent factor)  Other virulent factors / toxins: Pneumolysin, hemolysin or fibrinolysin
	Diseases	 MOPS → Meningitis, Otitis Media, Pneumonia, Sinusitis  especially in Splenectomised individuals  Most common cause of Post influenza pneumoniae followed by <i>Staph Aureus</i>  Vaccinate the Individuals to be Splenectomised → 2 – 4 weeks prior to Splenectomy (2 weeks at least).  In emergency cases - Vaccinate 4 weeks after Splenectomy
	Diagnosis	 Sputum Culture, blood culture and antigen detection  Rusty Brown in Pneumonia caused by <i>S pneumoniae</i>

GRAM -VE COCCI	NEISSERIA MENINGITIDIS (MENINGOCOCCUS)	N. GONORRHEA (GONORRHEA) -- DIPLOCOCCI
Route Of Transmission	<ul style="list-style-type: none"> Respiratory/oral secretions Common in army barracks / Nurseries 	<ul style="list-style-type: none"> Sexual (STD) / Transplacental Heterosexual route more common than homosexual.
Capsule	<ul style="list-style-type: none"> Polysaccharide capsule 	<ul style="list-style-type: none"> No capsule but pilus present
Fermentation	<ul style="list-style-type: none"> Mannitol fermenter 	<ul style="list-style-type: none"> Glucose fermentation
Vaccine	<ul style="list-style-type: none"> Available (type B) 	<ul style="list-style-type: none"> No Vaccine
Virulence Factors/Toxins	<ul style="list-style-type: none"> Lipo-Oligosaccharide LOS IgA protease, Outer membrane proteins 	<ul style="list-style-type: none"> LOS (major virulent factor) IgA protease, No Vaccine due to antigenic variation of pilus
Diseases	<ul style="list-style-type: none"> meningococcaemia/shock Waterhouse Friedrichsen syndrome (fever & acute adrenal insufficiency + DIC) 	<ul style="list-style-type: none"> Gonorrhoea Septic Arthritis Neonatal conjunctivitis PID (chlamydia more common) Fitz Hugh Curtis syndrome (chlamydia > Gonorrhoea)
Diagnosis	<ul style="list-style-type: none"> Culture & PCR 	<ul style="list-style-type: none"> Nucleic Acid amplification test NAAT gold standard
Prevention & Prophylaxis	<ul style="list-style-type: none"> Rifampin > Cipro/ Ceftriaxone 	<ul style="list-style-type: none"> Use of condoms decreases transmission. Erythromycin eye ointments to decrease neonatal blindness
Treatment	<ul style="list-style-type: none"> Penicillin G is DOC Ceftriaxone 	<ul style="list-style-type: none"> Ceftriaxone is DOC Add Azithromycin for coinfection with Chlamydia
GRAM + VE RODS		
Listeria Monocytogens	<ul style="list-style-type: none"> Tumbling / shooting star motility. Sensitive to Ampicillin. Inf occurs by ingestion of Unpasteurized / raw Milk. Deli meats. Also called Refrigerator worm. May cause Neonatal Sepsis, Meningitis in extreme of ages, Amnionitis and granuloma infantiseptica 	
Corynebacterium Diphtheriae	<ul style="list-style-type: none"> Respiratory route. Exotoxin inhibits protein synthesis via EF-2 inhibition Club shaped. Palisading growth pattern Black colonies on Tellurite agar Metachromatic; red, blue granules are formed by it Tellurite agar > Löffler Medium for diagnosing Pseudomembranous pharyngitis (Bull neck appearance) Diphtheria infects CD8+ cells. Throat swab is used for diagnostic purposes Toxic to Heart (toxic Myocarditis) and Nerves (cranial nerves palsies e.g., Facial Palsy) Treat by anti-toxin and Erythromycin / Penicillin 	
Bacillus Spp. (Spore forming obligate aerobe)	B. Anthrax	<ul style="list-style-type: none"> Tennis racket shaped. Cutaneous anthrax 90% of cases. Wool sorter's disease when infection occurs in lungs. Present with Widened mediastinum on CXR Maffay stain is used for Capsule. Capsule is of Poly D glutamate. Colonies are of Medusa head appearance Blood agar can be used for growth of B. anthrax Prophylaxis with Ciprofloxacin. Anthrax toxin consists of Lethal factor, edema factor and protective antigen. Can be used as an agent of Bio war / Bio terrorism.

	B. Cereus	<ul style="list-style-type: none"> Causes Food poisoning enterotoxin causes Non bloody Diarrhea and emesis. Reheated Rice is the Most common source of infection. Antibiotics are ineffective
Clostridium Spp. (Spore forming obligate anaerobe)	C.Tetani	<ul style="list-style-type: none"> Produces Exotoxin > Neurotoxin Blocks GABA + Glycine release from Renshaw cells of Spinal cord. Affects Motor nerves. Spastic paralysis, Locks jaw, Risus Sardonius & Opisthoclonus are features. Prevention with Toxoid Vaccine Treat with wound washing, antibiotics, Toxoid, and immunoglobulins HIG preferred over ATS.
	C.Botulinum	<ul style="list-style-type: none"> Infant Botulism: by ingestion of Spores in Honey. Toxin produced in Vivo In adults: by Canned foods (Preformed toxin). Descending flaccid paralysis. Dysphagia. Diplopia may occur leading to Respiratory failure. Toxin inhibits Ach release at NMJ
	C.Perfringens	<ul style="list-style-type: none"> Produces Alpha toxin/ Lecithinase causing myonecrosis and enterotoxin causing food Poisoning by Reheated Meat. Also called Buffet germ. C. Welchii is imp cause of Gas Gangrene. Treated by Wound debridement and Penicillin
	C.Difficile	<ul style="list-style-type: none"> Produces toxin A, B. It is the important cause of Antibiotics associated diarrhoea e.g., Ampicillin, Clindamycin, cephalosporins/ Quinolones. Causes Pseudomembranous Colitis. Diagnoses by Stool - toxin determination and PCR. Treated by Metronidazole (oral) -- DOC. For severe cases use IV metronidazole and Oral Vancomycin For resistant cases use Vancomycin (orally) For recurrent cases: Faecal Microbiota transplant

GRAM +VE BRANCHING FILAMENTEOUS RODS	
NOCARDIA	ACTINOMYCES
<ul style="list-style-type: none"> Weakly Acid-fast aerobe found in Soil Causes Lung infections that can mimic T.b but -ve PPD Test Cutaneous inf can spread to CNS Causing Multiple Brain Abscesses Treated with Sulphonamides 	<ul style="list-style-type: none"> An anaerobe that is Normal Oral/ GIT flora Causes Oral/facial abscess with Multiple draining Sinuses Abscess with Granuloma, containing yellow sulphur granules These granules consist of Organisms Causes PID most commonly in females with IUDs Treated with Penicillin

ZIEHL NEELSEN (ZN) STAINING

- ❖ Acid fast organisms stain red, while the background remains blue.
- ❖ 3 bacilli are required for documenting acid fast. ZN stain confirms the acid-fast property of bacteria e.g., mycobacterium

i. Primary Stain	Apply Cabrol Fuchsin for 30 seconds
ii. Heat	Heat for 2min -- acts as Mordant/fixator. After Heat application, Cool it.
iii. Decolorizer	Add Acid alcohol for 15 seconds
iv. Counterstain	with 2ndry dye Methylene Blue

MYCOBACTERIUM

MYCOBACTERIUM TUBERCULOSIS		
Characteristics	<ul style="list-style-type: none"> ○ Acid-fast bacilli. Stains acid fast due to Mycolic acid in cell wall ○ Transmits via Respiratory route. Colonies are Rough, tough and bough. ○ Mycobacteria Tb may remain alive in sputum for 20 hrs. ○ Contains Cord factor which activates Macrophages and promoting Granuloma formation + TNF release. Sulfatides inhibit Phagocytosis 	
Clinical features	<ul style="list-style-type: none"> ❖ Fever, cough, hemoptysis, weight Loss / Meningeal signs in TBM ❖ Matted cervical Lymph nodes Nodes/Sinuses formation e.g., Neck ❖ Can present as GIT T.b from Unpasteurized Milk ❖ Primary T.b affects Posterior segment of Lower Lobe of Lungs. ❖ Ghon complex is seen. Ghon complex consists of Granuloma with surrounding Lymphatics ❖ Secondary T.B affects Apex Due to well oxygenated zone ❖ Cavitation seen in only secondary Tb. ❖ Calcification, +ve PPD, Caseating granuloma in both 1° and 2° Tb 	
Diagnosis	<ul style="list-style-type: none"> ✓ Chest X ray is initial investigation ✓ PPD/Mantoux Test: +ve if past exposure or current infection. Type 4 hypersensitivity reaction ✓ Histological analysis shows Epithelioid Cells ✓ Microscopic feature: Caseating Granuloma ✓ Diagnostic test : PCR > AFB. Sputum for AFB is the rapid most way ✓ Definitive Diagnosis Requires Sputum Culture ✓ Culture Media → Leven stein Jensen Agar. LJ agar or Middle Brook Media (Liquid Medium) ✓ Diagnosis of Extrapulmonary Tb requires Lymph Node Biopsy ✓ Margins of T.b Ulcer are Undermined, while Antibodies are Cell Bound 	
Complications	<ul style="list-style-type: none"> • Renal Tb – most common cause of Sterile Pyuria is Tb-- Followed by Chlamydia and gonorrhoea • Vertebrae (Pott's disease), Meningitis, Disseminated disease / Miliary tb and death. 	
Treatment	<p>Primary T.b heals in 90% cases by fibrosis/calcification</p> <p>1st line Drugs: RIPES</p> <p>Duration: 6 to 12 months. 6-9 month for Pulmonary Tb. 12-month for Tb meningitis</p> <p>Remember, 4-2-4 → 4 drugs for 2 months. 2 drugs for 4 months</p> <p>Rifampin: red orange secretion</p> <p>Isoniazid: Hepatotoxic and Peripheral Neuropathy. Add Pyridoxine/VitB6 60mg for neuropathy.</p> <p>Pyrazinamide: Gout + most hepatotoxic drug</p> <p>Ethambutol: Red, green color blindness. Affects vision.</p> <p>Streptomycin: nephrotoxic. Ototoxic</p> <p>2nd line Drugs</p> <p>Ethionamide (Thyroid problems), Ciprofloxacin, Amikacin, Capreomycin, PAS, rifabutin</p> <p>DOTS → Directly Observed Treatment Short Course is the best effective Care plan</p>	
Resistant TB	Multidrug Resistant T.B (MDR)	Resistant to both Isoniazid and Rifampin
	Extensive Drug Resistant (XDR)	Resistant to INH, Rifampin and among 2 nd line fluoroquinolones and injectables (Amikacin, kanamycin/ capreomycin) etc.
	Totally Drug resistant	Resistance to all drugs
	Mono-resistant	Mono-resistant -- only 1 drug resistance
	Polyresistant	resistant to more than 1 drug except isoniazid/Rifampin
Nontuberculous Mycobacterium	<p>Mycobacterium Marinum causes disease in Aquarium handlers</p> <p>Mycobacterium Scrofulaceum causes Scrofula/Cervical Lymphadenopathy</p>	
Mycobacterium Avium Intracellularae Complex	<p>MAC Causes Disseminated disease in AIDS when CD4 count < 50 cell/mm³</p> <p>Prophylaxis with Azithromycin when CD4 falls less than 50.</p>	
Mycobacterium Bovis	Causes Tb in cattle. GIT tb association. Tb vaccine contains Mycobacterium Bovis strain.	
Mycobacterium Lepae	<p>M Lepae is one of the slowest growing organisms. Infects Skin & Superficial Nerves.</p> <p>Reservoir of organism is Armadillos. M leprae is an intracellular acid-fast bacterium.</p>	

Organism causes Hansen disease / LEPROSY → Glove and stocking loss of senses. No motor Loss Leprosy Has 2 forms: tuberculoid/Lepromatous leprosy	
Tuberculoid LEPROSY	Lepromatous LEPROSY
<ul style="list-style-type: none"> high cell mediated immunity with large Th1 response. low bacterial load. Few hypoesthetic hairless skin plaques 	<ul style="list-style-type: none"> high Bacterial load with Low cell mediated Immunity and large Th2 response. Highly communicable form Diffuse Skin involvement with Lion like i.e., Leonine facies
Treated with Dapsone + Rifampin . Clofazimine for Lepromatous leprosy	
Diagnosis: Skin Biopsy / Nasal scraping /PCR	

DROPLET INFECTION	AIRBORNE INFECTION
<ul style="list-style-type: none"> 1-3 feet (less than 1 metre) Examples: Influenza, Rubella, Pertussis, Mumps, Meningitis, Pneumoniae Wear Surgical Mask while entering Room 	<ul style="list-style-type: none"> 3-6 ft / more than 1 metre Examples: Tb, measles & chicken pox etc Wear N-95 mask. Must have Private room.

MANTOUX TEST/ PPD TEST/TUBERCULIN TEST	<p>Type 4 Hypersensitivity reaction</p> <p>Intradermal injection of purified protein derivatives to look for Active / Latent T.b</p> <p>Induration is measured after 48-72 hrs. Note that Induration matters not erythema</p> <p><u>INTERPRETATION:</u></p> <ul style="list-style-type: none"> ✓ 15mm induration: Healthy individual / No risk factors ✓ 10mm induration: IV Drug abusers, Health personnel's, comorbid and children <4 yrs. ✓ 5mm induration: HIV+ve / Organ transplant, Close / Direct contacts, fibrotic changes on CXR <p>FALSE -VE TEST: Seen in Immunosuppression /Disseminated Tb, Recent Viral/ bacterial inf.</p> <p>FALSE +VE TEST: Seen in previous BCG Administration and Non-Tuberculous Mycobact inf.</p>
INTERFERON GAMMA RELEASE ASSAY / IGRA	Fastest highly sensitive test for rapid detection of Tb. May be false +ve in BCG administration.

GRAM -VE RODS

- ✓ **Lactose Fermenting Bacteria** form pink colonies on MacConkey Agar e.g., *E. coli*/ *Enterobacter* and *Klebsiella*.
- ✓ *E. coli*, *Enterobacter* and *Klebsiella* are fast fermenters. *Citrobacter* + *Serratia*-Slow Fermenter.
- ✓ **Non-Lactose Fermenters** may be **Oxidase +ve/-ve**. *Pseudomonas* is Oxidase +ve, whereas Oxidase -ve are further differentiated based on H₂S production on TSI Agar.
- ✓ *Salmonella* + *proteus* are Oxidase -ve that produce H₂S whereas, *Shigella* & *Yersinia* don't give H₂S.

E. Coli	<ul style="list-style-type: none"> Motile indole +ve rod. Forms Green sheen on EMB agar Virulence by: P pili (pyelonephritis), K Capsule (pneumonia + meningitis), Fimbria – cystitis LPS → Endotoxin-shock Most common cause of UTI + Pyogenic Liver abscess and Spontaneous bacteria Peritonitis. 2nd common cause of Neonatal Meningitis Ascitic tap contains E coli in SBP. 4 different strains of E. coli are pathogenic EHEC doesn't ferment Sorbitol. Rest all do <table border="1"> <tr> <td>Enteroinvasive E. Coli</td><td>Like shigella – it invades intestinal mucosa</td></tr> <tr> <td>Enterotoxigenic</td><td>produces Enterotoxins and causes Traveller's watery diarrhoea.</td></tr> <tr> <td>Enteropathogenic</td><td>causes diarrhoea and malabsorption in children</td></tr> <tr> <td>Enterohemorrhagic (EHEC)</td><td>via Shiga toxin by eating Hamburger/Undercooked meat/ raw vegetables cause Dysentery and Hemolytic Uremic syndrome. O157:H7 – most common serotype.</td></tr> </table>	Enteroinvasive E. Coli	Like shigella – it invades intestinal mucosa	Enterotoxigenic	produces Enterotoxins and causes Traveller's watery diarrhoea.	Enteropathogenic	causes diarrhoea and malabsorption in children	Enterohemorrhagic (EHEC)	via Shiga toxin by eating Hamburger/Undercooked meat/ raw vegetables cause Dysentery and Hemolytic Uremic syndrome. O157:H7 – most common serotype.
Enteroinvasive E. Coli	Like shigella – it invades intestinal mucosa								
Enterotoxigenic	produces Enterotoxins and causes Traveller's watery diarrhoea.								
Enteropathogenic	causes diarrhoea and malabsorption in children								
Enterohemorrhagic (EHEC)	via Shiga toxin by eating Hamburger/Undercooked meat/ raw vegetables cause Dysentery and Hemolytic Uremic syndrome. O157:H7 – most common serotype.								
Salmonella Spp.	<table border="1"> <tr> <td>S. Typhi</td><td> <ul style="list-style-type: none"> Human reservoir only, flagellated rod. Causes Typhoid fever: Fever of Step Ladder pattern+ Relative Bradycardia, constipation + Rose spots-7th day. S typhi Resides in Payer's Patches of ileum. May complicate to Intestinal Haemorrhage/Perforation in 3rd week Diagnosis Of Typhoid Fever -- Mnemonic: BASU 1st week- Blood. Culture-gold standard 2nd week- Ag/Ab- Serology (widal / Typhi dot test) 1: 160 Titres of O antigen is diagnostic 3rd week- Stool culture. 4th week- Urine culture Most sensitive test - Bone marrow aspiration. Carrier state: Gallbladder Colonization. Treatment: Ciprofloxacin 500mg 1× BD – 14 days Ceftriaxone / Azithromycin can also be used. For Prophylaxis & Carrier: Ciprofloxacin 500mg 1 × BD – 14 Days or 28 days regimen can also be used </td></tr> <tr> <td>Salmonella Spp. Except S. Typhi</td><td>They cause Gastroenteritis -- by consuming infected Poultry, eggs/pets. Endotoxin causes Bloody diarrhoea. Antibiotics are not indicated</td></tr> </table>	S. Typhi	<ul style="list-style-type: none"> Human reservoir only, flagellated rod. Causes Typhoid fever: Fever of Step Ladder pattern+ Relative Bradycardia, constipation + Rose spots-7th day. S typhi Resides in Payer's Patches of ileum. May complicate to Intestinal Haemorrhage/Perforation in 3rd week Diagnosis Of Typhoid Fever -- Mnemonic: BASU 1st week- Blood. Culture-gold standard 2nd week- Ag/Ab- Serology (widal / Typhi dot test) 1: 160 Titres of O antigen is diagnostic 3rd week- Stool culture. 4th week- Urine culture Most sensitive test - Bone marrow aspiration. Carrier state: Gallbladder Colonization. Treatment: Ciprofloxacin 500mg 1× BD – 14 days Ceftriaxone / Azithromycin can also be used. For Prophylaxis & Carrier: Ciprofloxacin 500mg 1 × BD – 14 Days or 28 days regimen can also be used 	Salmonella Spp. Except S. Typhi	They cause Gastroenteritis -- by consuming infected Poultry, eggs/pets. Endotoxin causes Bloody diarrhoea. Antibiotics are not indicated				
S. Typhi	<ul style="list-style-type: none"> Human reservoir only, flagellated rod. Causes Typhoid fever: Fever of Step Ladder pattern+ Relative Bradycardia, constipation + Rose spots-7th day. S typhi Resides in Payer's Patches of ileum. May complicate to Intestinal Haemorrhage/Perforation in 3rd week Diagnosis Of Typhoid Fever -- Mnemonic: BASU 1st week- Blood. Culture-gold standard 2nd week- Ag/Ab- Serology (widal / Typhi dot test) 1: 160 Titres of O antigen is diagnostic 3rd week- Stool culture. 4th week- Urine culture Most sensitive test - Bone marrow aspiration. Carrier state: Gallbladder Colonization. Treatment: Ciprofloxacin 500mg 1× BD – 14 days Ceftriaxone / Azithromycin can also be used. For Prophylaxis & Carrier: Ciprofloxacin 500mg 1 × BD – 14 Days or 28 days regimen can also be used 								
Salmonella Spp. Except S. Typhi	They cause Gastroenteritis -- by consuming infected Poultry, eggs/pets. Endotoxin causes Bloody diarrhoea. Antibiotics are not indicated								
Shigella	<p>S. dysenteriae invades M cells. Very low infectious dose is pathogenic. Spreads by Finger, Flies, Food, Faeces. Reservoir-Human only</p> <p>Bacillary dysentery: crampy Abdominal pain, tenesmus + Bloody Mucoïd stools.</p> <p>Treated by Ciprofloxacin 500mg 1×BD × 03 days</p>								
Klebsiella	<p>Intestinal Opportunistic rod. Thick Mucoïd Capsule Red Currant jelly sputum</p> <p>Pneumoniae in Alcoholic / Diabetic when aspirated. May cause nosocomial UTI.</p>								
Proteus	<p>Motile rod, Urease +ve, Swarming Motility. 2nd commonest cause of UTI. May give rise to Staghorn stone (Mg-Ammonium Phosphate stone)</p>								
Legionella Pneumophila	<ul style="list-style-type: none"> Aerosol Transmission from ACs / water tanks. Smoking/Old age are risk factors Use Silver stain as it gram stains poorly. Grows on Charcoal Yeast extract medium with iron + Cysteine Potanic Fever: mild flu like illness Legionnaire's disease: Fever + pneumoniae + CNS + GI symptoms May cause Pneumoniae with Hyponatremia Detected by Urine antigen Test 								
Pseudomonas Aeruginosa	<ul style="list-style-type: none"> Opportunistic, Catalase +ve, Oxidase +ve, Motile rod having Fruity grape like Odour. Found in Water. Produces Pigments pyoverdine, Pyocyanin- (blue green) Exotoxin A, Endotoxin and Phospholipase C and capsule are virulence factors. Gentamycin is most effective against it whereas Quinolones -now least effective May cause Pneumonia/Sepsis in Diabetics, Cystic fibrosis/ Burn patients. Ventilator associated pneumonia. Sepsis in IV drug abusers UTI- nosocomial (2nd common cause of Hospital Acquired infections after Staph. Aureus) Wound infection in burn victims. Hot tub folliculitis / Skin infections Otitis Externa (Swimmer's ear). Corneal Ulcers in Contact Lens wearers Ecthyma Gangrenosum: necrotic skin lesion 								

GRAM -VE CURVED RODS

(H. Pylori, Vibrio Cholera, Campylobacter Jejuni)

Helicobacter Pylori (H. Pylori)	Characteristics	Triple +ve curved flagellated rod. Catalase +Oxidase+ Urease +ve, colonizes Antrum. Survives at low PH ≤ 2.5 in the acidic environment. Virulence by CagA, VacA genes.	
	Risk factors	Commonly acquired in childhood, Poor socioeconomic status, Poor Hygiene, Overcrowding and restaurants’ meal consumption	
	Diseases	Gastritis, Ulcer and Cancer (MALTOMA) Peptic ulcer location: 1 st part of duodenum most commonly and Lesser curvature of stomach for gastric ulcer. MALTOMA= Mucosa associated Lymphoid tissue lymphoma Symptoms of peptic ulcer include Dull abdominal pain more at night, Bloating, Burping, bad breath, indigestion, Unexplained weight Loss/ Iron def anemia	
	Investigations	Invasive	Urease test, Biopsy, Culture / PCR. Blood Culture-gold standard
		Non invasive	Urea breath test, Serology, Stool Antigen test. Test for Eradication: Urea breath Test. Don’t use serology. Stool Ag test can also be used. Serology is most commonly used test, but it is useful only if never treated for H. pylori before.
	Treatment	Quadruple therapy is gold standard. But commonly used is triple regimen – 14 days Triple Regimen: APC = Amoxil, PPI, Clarithromycin In case of Amoxicillin allergy, use Metronidazole. Quadruple Regimen: APC + Metronidazole OR TOMB: Bismuth regimen for clarithromycin resistance : Tetracycline + Omeprazole + Metronidazole + bismuth	
Complications	Peptic Ulcer can Bleed (most commonly), perforate /may cause Obstruction. Risk of Gastric cancer i.e., Gastric Lymphoma inc. Only Tumor that can be treated by Antibiotics		
Vibrio Cholera	comma shaped, oxidase + flagellated acid labile rod. Grows well in Alkaline medium i.e.(Resistant to Alkaline Media). Source -- Sea foods (fish) or Contaminated water Causes Watery Diarrhea with Rice water stools. It can be Fatal. Treat by ORT + Erythromycin/Clarithromycin.		
Vibrio Vulnificus	Causes necrotizing skin infections due to contaminated sea water especially in CLD pts		
Campylobacter Jejuni	Comma/ S shaped Polar flagellated. Grows at 42 C°. Major cause of Bloody diarrhoea in children by ingestion of Undercooked Meat / unpasteurized Milk Associated with Guillain barre syndrome, Reactive Arthritis Macrolides are drug of choice -- Erythromycin / Azithromycin		

GRAM -VE COCCOBACILLUS

(H. influenza, Bordetella, Brucella, Yersinia, Francisella, Pasteurella)

Haemophilus Influenzae	<ul style="list-style-type: none"> Metallic sheen Coccobacillus Aerosol transmission, Produces IgA protease Cultured on Chocolate agar with factor V (NAD+) and factor X (Hematin), Conjugated Vaccine --- Vaccine contains type b capsular polysaccharide. Diseases: pneumonia, otitis media, conjunctivitis, Epiglottitis Acute epiglottitis: cherry red epiglottis, drooling saliva, thumb sign on lateral x ray neck. Diagnosis -- blood culture. Treated with Amoxil + clavulanate. Ceftriaxone for meningitis by H. influenza. 						
Bordetella Pertussis	<ul style="list-style-type: none"> Pertussis toxin, tracheal toxin and adenylate cyclase toxin cause virulence. Grows on Bordet-gangauo agar Non-invasive. Nasal + respiratory secretions are contagious Causes whooping cough- 100 days cough. Cough + Post tussive Emesis (vomiting) Clinical stages: 3 → Catarrhal, Paroxysmal, Convalescent Catarrhal stage is highly infectious Treatment -- Macrolides 						
Brucella	<ul style="list-style-type: none"> Transmitted via Unpasteurized Milk Infects + survives in Reticuloendothelial system. Causes brucellosis: Swinging/Undulating fever, arthralgia, night sweats. Doxycycline is DOC. 						
Yersinia Spp	<p>Pleomorphic rod/Coccobacillus. Three main pathogenic species are as follows:</p> <table border="1"> <tr> <td>Yersinia Pestis</td><td>Rat flea is the vector Causes Plague -- (Pneumonic, Bubonic, septicaemic)</td></tr> <tr> <td>Yersinia Enterocolitia</td><td>Transmission via Pet faeces Causes dysentery + Pseudo-appendicitis</td></tr> <tr> <td>Yersinia Pseudotuberculosis</td><td>Causes Mesenteric Lymphadenitis, reactive arthritis</td></tr> </table>	Yersinia Pestis	Rat flea is the vector Causes Plague -- (Pneumonic, Bubonic, septicaemic)	Yersinia Enterocolitia	Transmission via Pet faeces Causes dysentery + Pseudo-appendicitis	Yersinia Pseudotuberculosis	Causes Mesenteric Lymphadenitis, reactive arthritis
Yersinia Pestis	Rat flea is the vector Causes Plague -- (Pneumonic, Bubonic, septicaemic)						
Yersinia Enterocolitia	Transmission via Pet faeces Causes dysentery + Pseudo-appendicitis						
Yersinia Pseudotuberculosis	Causes Mesenteric Lymphadenitis, reactive arthritis						
Francisella Taulerensis	<ul style="list-style-type: none"> transmitted by Tick bite-actually Tick's poop. Causes Tularaemia / Rabbit Fever. Symptoms include ulcerative skin lesions, fever, headache, myalgias, pneumonia Diagnosed by Culture. Treated by Aminoglycosides 						
Pasturella Multocida	<ul style="list-style-type: none"> P for Pasteurella and Pets. Transmission via cat / dog bite Causes Cellulitis which occurs within 24 hrs of bite / scratch. Can progress to necrotizing fasciitis or osteomyelitis Can be grown on Blood agar Treated by Augmentin / Calamox 						

GARDENELLA VAGINALIS	MYCOPLASMA PNEUMONIAE
<ul style="list-style-type: none"> Gram-variable Rod that causes Vaginosis It is NOT an STD, but linked to sexual activity Fishy odour of Vaginal discharge, enhanced by mixing with KOH i.e., called Amine-whiff test Clue cells are present Vaginal PH > 4.5 Treatment with Metronidazole 	<ul style="list-style-type: none"> Lacks cell wall-not gram stained Membrane has Sterols Grows on Eaton agar. Causes Walking Pneumoniae/atypical pneumonia, associated with High titres of cold agglutinins. Most common cause of pneumonia in young adults Especially in military personnel/colleges/prisons. Associated with Steven Johnson's syndrome, erythema Nodosum, autoimmune hemolytic anemia

SPIROCHETES

(Spiral shaped: Treponema Pallidum, Borrelia burgdorferi, Leptospira)

Treponema Pallidum	<p>Not gram stained because too thin to be visualized. Syphilis is caused by T pallidum Stages of syphilis are as follows :</p> <table border="1"> <tr> <td data-bbox="516 352 779 415">Primary syphilis</td><td data-bbox="787 352 1497 415"> <ul style="list-style-type: none"> • Painless chancre. P for Primary + Painless • Sample from genital lesion -- Scraping can be taken for diagnosis. </td></tr> <tr> <td data-bbox="516 415 779 567">Secondary syphilis</td><td data-bbox="787 415 1497 567"> <ul style="list-style-type: none"> • Maculopapular rash on Palm & Soles. • Condyloma Lata (smooth Painless wart like lesion) • Painless Lymphadenopathy. • May be followed by Latent Syphilis • Latent syphilis: +ve serology without symptoms. </td></tr> <tr> <td data-bbox="516 567 779 598">Tertiary syphilis</td><td data-bbox="787 567 1497 598"> <ul style="list-style-type: none"> • Gummas, aortitis, Tabes dorsalis, Argyll Robertson Pupil </td></tr> <tr> <td data-bbox="516 598 779 661">Congenital Syphilis</td><td data-bbox="787 598 1497 661"> <ul style="list-style-type: none"> • Hutchinson teeth, Mulberry, Sabir shins, rhagades, snuffles and deafness. Placental transmission occurs after 1st trimester. </td></tr> </table> <p>Diagnosis:</p> <table border="1"> <tr> <td data-bbox="516 693 698 724">Direct testing</td><td data-bbox="706 693 1497 756"> Dark field microscopy and PCR Dark Field microscopy for Primary + secondary syphilis is confirmatory. </td></tr> <tr> <td data-bbox="516 756 698 787">Serology</td><td data-bbox="706 756 1497 966"> Non-specific: RPR + VDRL VDRL may be used for Congenital syphilis but more specific is IgM FTA-ABS False +ve VDRL in Leprosy/ Lupus (anticardiolipin antibodies) Specific: FTA-ABS & TPPA. FTA-ABS: most specific + confirmatory test. Also, for Tertiary syphilis IgM-FAT Abs for Congenital syphilis diagnosis </td></tr> </table> <p>Treatment: Penicillin G Jarish Herxheimer reaction: flu like symptoms after antibiotics are started</p>	Primary syphilis	<ul style="list-style-type: none"> • Painless chancre. P for Primary + Painless • Sample from genital lesion -- Scraping can be taken for diagnosis. 	Secondary syphilis	<ul style="list-style-type: none"> • Maculopapular rash on Palm & Soles. • Condyloma Lata (smooth Painless wart like lesion) • Painless Lymphadenopathy. • May be followed by Latent Syphilis • Latent syphilis: +ve serology without symptoms. 	Tertiary syphilis	<ul style="list-style-type: none"> • Gummas, aortitis, Tabes dorsalis, Argyll Robertson Pupil 	Congenital Syphilis	<ul style="list-style-type: none"> • Hutchinson teeth, Mulberry, Sabir shins, rhagades, snuffles and deafness. Placental transmission occurs after 1st trimester. 	Direct testing	Dark field microscopy and PCR Dark Field microscopy for Primary + secondary syphilis is confirmatory.	Serology	Non-specific: RPR + VDRL VDRL may be used for Congenital syphilis but more specific is IgM FTA-ABS False +ve VDRL in Leprosy/ Lupus (anticardiolipin antibodies) Specific: FTA-ABS & TPPA. FTA-ABS: most specific + confirmatory test. Also, for Tertiary syphilis IgM-FAT Abs for Congenital syphilis diagnosis
Primary syphilis	<ul style="list-style-type: none"> • Painless chancre. P for Primary + Painless • Sample from genital lesion -- Scraping can be taken for diagnosis. 												
Secondary syphilis	<ul style="list-style-type: none"> • Maculopapular rash on Palm & Soles. • Condyloma Lata (smooth Painless wart like lesion) • Painless Lymphadenopathy. • May be followed by Latent Syphilis • Latent syphilis: +ve serology without symptoms. 												
Tertiary syphilis	<ul style="list-style-type: none"> • Gummas, aortitis, Tabes dorsalis, Argyll Robertson Pupil 												
Congenital Syphilis	<ul style="list-style-type: none"> • Hutchinson teeth, Mulberry, Sabir shins, rhagades, snuffles and deafness. Placental transmission occurs after 1st trimester. 												
Direct testing	Dark field microscopy and PCR Dark Field microscopy for Primary + secondary syphilis is confirmatory.												
Serology	Non-specific: RPR + VDRL VDRL may be used for Congenital syphilis but more specific is IgM FTA-ABS False +ve VDRL in Leprosy/ Lupus (anticardiolipin antibodies) Specific: FTA-ABS & TPPA. FTA-ABS: most specific + confirmatory test. Also, for Tertiary syphilis IgM-FAT Abs for Congenital syphilis diagnosis												
Borrelia Burdogferi	<ul style="list-style-type: none"> • Ixodes deer tick- vector. Mouse is natural reservoir • Antigenic variation by Outer surface protein • B Burdogferi causes Lyme disease. LYME DISEASE has 3 stages. <ul style="list-style-type: none"> Stage 1: Erythema migrans- bulls eye lesion. Stage 2: AV blocks, Facial palsy, arthritis – it is transient. Stage 3: Chronic arthritis, neuropathy • Diagnosis: PCR. Treatment with Doxycycline 												
Leptospira Interrogans	<ul style="list-style-type: none"> Found in water contaminated with Animal or Rat Urine. Diseases: leptospirosis / Weil's disease Leptospirosis: flu like illness, conjunctival injection, photophobia, calves myalgias, jaundice Weil's / soldier's disease: hepato-renal syndrome → jaundice+ azotemia from liver - kidney dysfunction. Fever, anemia, and bleeding Diagnosed by microscopic agglutination test- mat / PCR / indirect haemagglutination Treated with doxycycline / penicillin 												

Bacteroides Vs Provetella

(Gram -ve rods -Anaerobes)

- Bacteroides cause Abscesses below Umbilicus (B for Bacteroides & below) and Pyogenic peritonitis
- Provetella cause abscesses Above umbilicus and gingival/ periodontal infection
- Granuloma formation is not a feature of Anaerobe infection. Foul smelling discharge is characteristic
- Metronidazole is DOC for Bacteroides or anaerobes. Clindamycin is alternative drug.

OBLIGATE INTRACELLULAR BACTERIA

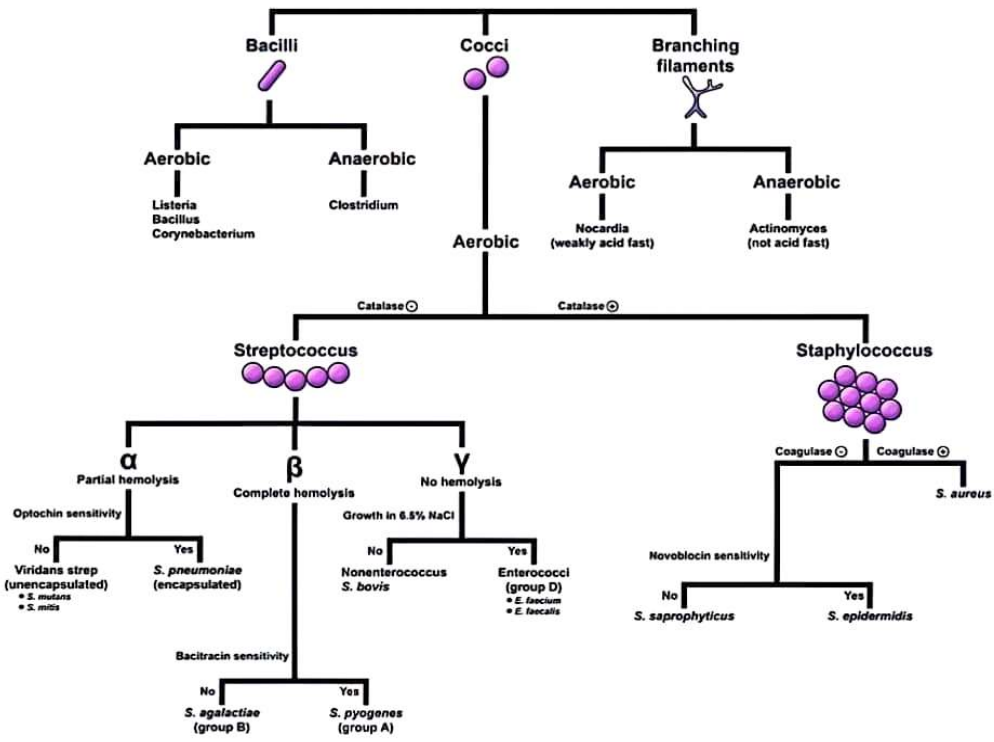
Chlamydia, Rickettsia, Coxiella, Ehrlichiosis, Anaplasmosis. Virtually they are gram -ve rods but depend upon Host ATP for survival.

Chlamydia	Cell wall lacks classic peptidoglycan, not gram stained, and beta lactam drugs are ineffective against them	
	Chlamydia psittaci	Psittacosis (Atypical pneumonia) in Bird keepers/breeders e.g., Pigeons
	Chlamydia pneumoniae	Atypical pneumonia
	Chlamydia trachomatis	20 serotypes as follows; Types A-C: Trachoma: MCC of preventable blindness, Chronic infections. Types D-K: Ophthalmia neonatorum – MCC Abnormal Vaginal or Urethral Discharge Pelvic inflammatory disease (female)--MCC Sexually Transmitted infection: MCC is chlamydia Also causes Sterile Pyuria: Culture negative. Types L1-L3: Lymphogranuloma venereum (LGV): Painless ulcer + painful lymph nodes
	Diagnosis	PCR / NAAT Cytoplasmic inclusions - on Giemsa stain
	Treatment	Azithromycin – DOC (single dose only). Alternative is Doxycycline Add Ceftriaxone for gonorrhoea co-infection.
Rickettsia	Rickettsia Rickettsi	Cause of rocky mountain spotted fever → Triad of Fever + headache + Rash Rash of Rocky Mountain Spotted fever involves Palm & Soles, whereas Rash of typhus spares Palm and Soles but involves Trunk Treatment Rickettsia with Doxycycline
	Rickettsia Prowazekii	causes Epidemic Typhus (vector--Louse)
	Rickettsia Typhus	causes endemic typhus (Flea vector)
	Rickettsia Tsutsugamushi	scrub typhus (Mite vector)
	Diagnosis and Treatment	Serology is diagnostic. Treatment – doxycycline
Coxiella	<ul style="list-style-type: none"> ➤ Coxiella burnetii -- not included in rickettsia ➤ No arthropod vector/ rash. Causes Q fever and culture - ve endocarditis ➤ Aerosol transmission e.g., from amniotic fluid of cattle/sheep etc. ➤ Serology is diagnostic 	
Ehrlichiosis Vs Anaplasmosis	<ul style="list-style-type: none"> ➤ Vector of both is tick ➤ Ehrlichiosis diagnostic feature is Monocytes with morula (cytoplasmic inclusions) Whereas, ➤ For anaplasmosis – Granulocytes with Morula ➤ Remember it as -- MEGA. <p>Monocytes → in Ehrlichiosis, while Granulocytes → in anaplasmosis</p>	

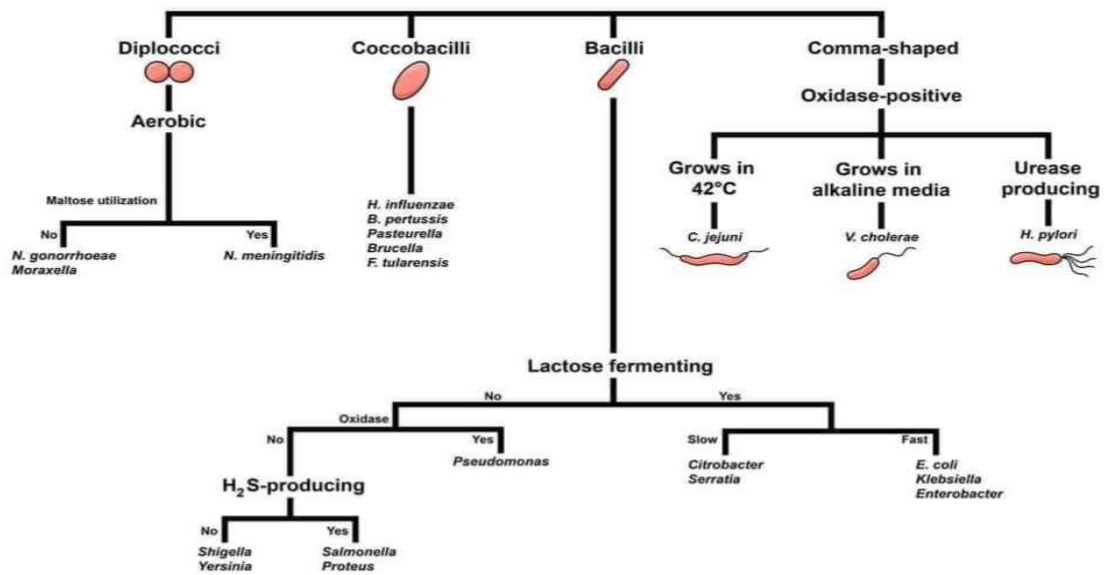
Remember That:

- Human Bite transmits *Eikenella corrodens* (gram -ve rod)
- Knuckle / fist fight as in Boxers -- transmits *Kingella* infection (gram -ve rod)
- *Fusobacterium* is an anaerobic normal oral flora that causes post angular sepsis called Lemmerie's disease

Gram-Positive Bacteria



Gram-Negative Bacteria

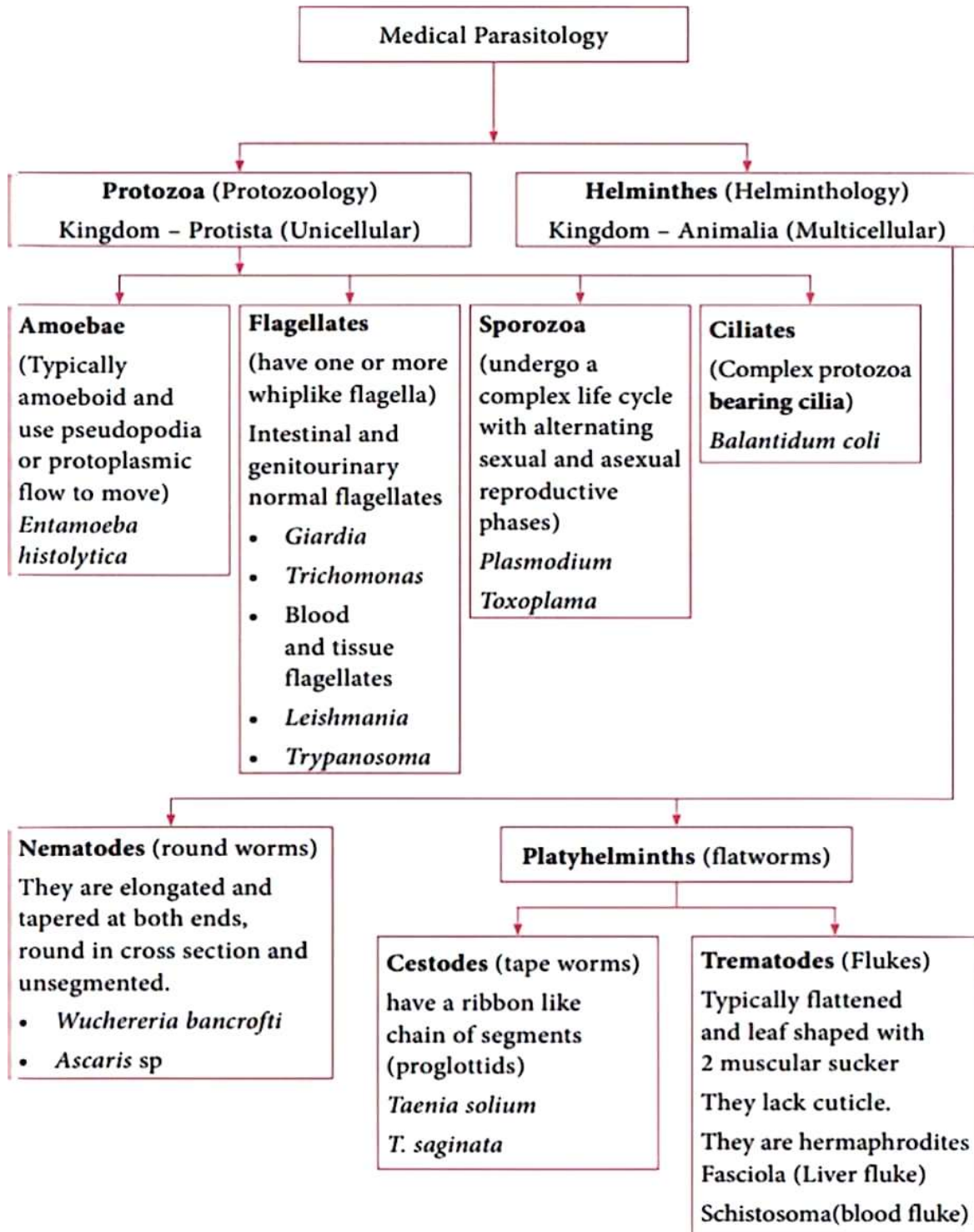


PAST PAPER BCQs OF BACTERIOLOGY

- Ascitic tap + Peritonitis – E. coli.
- Pyogenic peritonitis – Bacteroides. Abdominal and gynaecological infection – Bacteroides.
- Prozone phenomena is due to high antibody titres.
- Abscess /Acute osteomyelitis/ Toxic shock syndrome –S. Aureus.
- Wound infection – S. Aureus > Pseudomonas
- Hospital acquired pneumonia – S. Aureus.
- Septic meningitis – Streptococcus Pneumoniae
- Initiation of dental caries – Streptococcus.> Lactobacillus
- Pyogenic lung abscess + Meningitis – Staphylococcus.
- Subacute bacterial endocarditis – S. viridians.
- Prosthetic valve endocarditis – S. epidermidis.
- Cellulitis/ Scarlet Fever – S. pyogenes.
- Multiple draining sinuses /IUCD infection Actinomycosis.
- Trachoma /Pelvic inflammatory disease /Lymphogranuloma venereum -Chlamydia.
- Pseudomembranous colitis – C. Difficile.
- Gas gangrene – C. Perferingens / **C. Welchii**.
- Fatal diarrhoea /rice water stools– V. Cholera.
- Grows on 42 C°- Campylobacter jejuni
- Tubo- ovarian cyst / Non-Ulcerative Lesion on genitals– Gonococcus.
- Rice water Stool- Cholera
- Reheated Rice- B. Cereus
- Sore throat+ facial palsy- C. Diphtheria
- Most common cause of UTI- E. Coli, 2nd Common cause of Uncomplicated UTI= S. Saprophyticus
- Tetanus toxin is EXOTOXIN > NEUROTOXIN
- C. Difficile has Toxin A & B. STERILE PYURIA: TB > Chlamydia & Gonorrhoea
- S. typhi resided in Peyer patches and carrier in gallbladder
- Pneumococcus Capsule is most potent virulent factor. Toxins are Pneumolysin/hemolysin/fibrinolysin
- Protein A is most imp Virulent factor for staph Aureus
- Metronidazole is DOC for Bacteroides + C. difficile
- Q fever Coxiella has no arthropod vector and Amniotic fluid of cattle is the source
- Sterile Pyuria- MCC is Tb followed by Chlamydia and gonorrhoea
- PID- Most common cause is Chlamydia
- Urethral discharge+ Non ulcer lesion- Gonorrhoea
- Congenital syphilis is diagnosed by IgM-FTA ABS
- Primary+ 2nd dry syphilis by DARK FIELD MICROSCOPY
- Penicillin G is Doc for Syphilis
- Doxycycline is DOC for Brucella, borrelia and rickettsia
- Azithromycin is DOC for mycoplasma and chlamydia
- Legionella is diagnosed by Detection of Ag in Urine
- Leptospira is found in water contaminated with Animal / rat urine
- Genital scraping from genital lesion helps in diagnosing primary syphilis
- Mesosomes are organelles present in bacteria for respiration
- Plasmid is small Circular, double stranded DNA independent of chromosomes.
- Mycoplasma pneumonia Causes Walking Pneumoniae
- Antibiotics effect the LOG phase of bacterial growth
- No chromosomal DNA is transferred by conjugation
- High titres of cold agglutinins. MCC of pneumonia in young adults-mycoplasma
- Test for Eradication of H. pylori: Urea breath Test.
- E. coli is commonest cause of Traveller's diarrhoea (by Toxigenic strain)

- Granuloma formation is not a feature of Anaerobe infection
- Rat flea is the vector for plague.
- 15mm induration: Healthy individual / No risk factors
- Motile indole +ve rod Forms Green sheen on EMB agar is E COLI
- Grows well in Alkaline medium i.e. (resistant to Alkaline Media) Is VIBRIO cholera
- Pneumoniae in Alcoholic / Diabetic when
- Definitive diagnosis: Requires Sputum Culture for TB
- Droplet infection: 1-3 feet; Airborne infection: 3-6 ft / more than 1 metre.
- C. Perfringens is due to Re heated meat
- Syphilis causes Painless Ulcer and painless lymph Nodes
- Mayonnaise / pastries/ pastas related infection- staph. Aureus
- Painless Ulcer+ painful Lymph Node= Lymphogranuloma venereum
- Dec Tendon reflexes is not a feature of Leprosy
- Given ATT for 02 months, now moderately elevated ESR- cause is Anemia
- If ESR is high (not moderately): prefer Superimposed bacterial infection
- Schwartz phenomena is due to Endotoxin reaction
- Pseudomonas cause fever by TNF; Overall Fever: IL-1 > TNFA
- Rickettsia differs from mycoplasma by Giemsa stain
- STD by Chlamydia > Gonorrhoea > syphilis
- Leprosy diagnosed by Nasal scraping
- Diphtheria is lethal to heart and nerves
- Catalase +ve, coagulase -ve causing infection after CVP – Staph Epidermidis.
- Staph aureus escapes phagocytosis by Protein A > Efb (extracellular fibrinogen binding protein)
- Staph aureus differentiated from others by Coagulase +ve
- Fever and chills + yellow sputum – staph. Aureus
- Profuse diarrhoea+ shooting star motility-vibrio cholera
- Triad of hepatomegaly+ sinus bradycardia + leukopenia- Typhoid
- H. influenza is normal flora of respiratory tract
- Puerperal sepsis by: GBS > E coli > Bacteroides
- Diphtheria grows at Tellurite agar > Loffler medium
- Post influenza most common organism is S pneumoniae > staph aureus
- Pneumococcus is MCC of post splenectomy sepsis and E. coli is least common cause
- Gram -ve differ from gram +ve by Periplasmic space
- Gram +ve differ from negative by thick peptidoglycan / thick cell wall and teichoic acid
- Capsule increases virulence / toxicity
- Yellow discharge+ grape like clusters- staph aureus _ abscess in both Lungs
- Abdominal pain + persistent vomiting after eating out- Staph aureus ENTEROTOXIN
- B. anthrax grows in blood agar and Maffay stain used for capsule of anthrax
- Young labour presents with Dysuria +urethritis – chlamydia is cause
- Enterotoxigenic E. coli causes Traveller's diarrhoea
- Yellow granules= Actinomyces whereas yellow Colonies= staph aureus
- Diphtheria affects CD8+ Cells
- Male develops diarrhoea from a stream water along with 2 children- vibrio cholera
- Watery diarrhoea that resolves after 1 week- Rota virus
- Foul smelling / fatty diarrhoea that resolves itself- Giardia Lamblia
- Urethral discharge shows gram-ve diplococci= N. gonorrhoea
- TSS by staph aureus causes—Skin desquamation
- Butchers are at high risk of developing Brucellosis.
- Brucella is gram -Ve Coccobacillus
- Sick cell disease pt presents with Osteomyelitis= Salmonella infection
- Rash on palm+ soles + painless lymphadenopathy= secondary syphilis

- Endotoxin causes Complement activation
- Mycolic acid/ cell wall composition provides virulence to Tb
- Tb is an airborne preventable disease.
- Enterococcus is gram +ve diplococci
- Fishy odour+ thin white discharge- bacterial Vaginosis
- Post abortion sepsis: Grp B streptococcus > E. coli > Bacteroides
- Trachoma is MC infectious preventable cause of blindness
- Follicular conjunctivitis is feature of trachoma
- IV drug abuser with fever, hypotension, and needle track sign= Pseudomonas
- Serosanguinous vaginal discharge after sore throat –Streptococcus pyogenes
- ASO titre is helpful in diagnosing Rheumatic fever
- Release of Phospholipase/Lecithinase causes gangrene by C. perferingens
- Bloody Diarrhea+ curved rod grows on 42C = C. jejuni
- Young male with fever, cough, joint pain, TLC normal= Mycoplasma pneumonia
- Staph aureus& klebsiella are opportunistic organism
- Mycobacterium Leprae is intracellular AFB
- Cholera decreases Neutral Nacl absorption
- Tetanus toxin decrease GABA and glycine release from NMJ
- Gram+ ve catalase +ve coagulase -ve causing UTI= Staph saprophyticus
- DOC for resistant and severe C. difficile is Vancomycin
- Virulence of bacteria depends on Type of toxin and No. of organisms
- Fever and hypotension in gram-ve is due to Endotoxin
- Drug of choice for Acinetobacter bumanii = Imipenem
- Shigella causes Mucosal invasion via M cells
- Atypical mycobacteria are resistant to Anti Tb drugs
- Neonate having fever, neck rigidity- Grp B Strep > E. coli > Listeria
- Alcoholic pt + pneumonia + air fluid levels on CXR=Klebsiella
- Pt having deep neck infection= cause is Mixed aerobes
- Child with abd Pain + Stool having Pus and RBCs= EIEC > ETEC
- Proteus, H. pylori + Nocardia + klebsiella= Urease +ve

PARASITOLOGY






HOST PARASITE RELATIONSHIPS




Parasitism	Parasite is fully dependant on host, harms the host and can't live independently.
Commensalism	Parasite drives benefit from host, doesn't harm the host & can live independently.
Symbiosis / Mutualism	Both host & parasite are dependent on each other without harming.

TYPES OF HOSTS

Definitive Host	Host in which parasite reaches sexual maturity (Sexual reproduction)
Intermediate Host	Parasite is metabolically dependant on Host. Asexual reproduction occurs.
Parentic Host	A transport host, parasite doesn't require it to complete life cycle.
Reservoir Host	Harbours population of parasite and can transmit it to others.

PROTOZOA

Entamoeba Histolytica	<ul style="list-style-type: none"> Two forms: Cysts (inactive) & Trophozoite (active) (4 nuclei in trophozoite) Transmission via Ingestion of Cyst in contaminated water. More common in homosexual male. E. histolytica is pathogenic whereas entamoeba coli is NON pathogenic amoeba <p>Diseases:</p> <ol style="list-style-type: none"> Amoebic Dysentery (Bloody diarrhoea, Crampy abdominal pain & tenesmus. May have Fever Flask shaped ulcers on colon biopsy Liver abscess -- Anchovy paste appearance Lung abscess i.e., via direct extension from Liver Brain abscess <p>Diagnosis & Treatment:</p> <ul style="list-style-type: none">  Stool examination Via Wet /Iodine preparation Shows RBCs in Trophozoites. Cysts are found in formed stools  Periodic acid Schiff staining  Serological studies: Indirect Haemagglutination assay / ELISA Especially for invasive infection or Extra intestinal infection (Liver abscess)  PCR  Rx with Metronidazole and luminal agents: diloxanide furoate/ Paromomycin/ iodoquinol
Giardia Lamblia	<ul style="list-style-type: none"> 4pairs of Flagella + 2 nuclei in trophozoite Two forms same as amoeba Transmission via ingestion of Cysts in water especially in Hikers using stream water <p>Disease Giardiasis - Watery foul-smelling diarrhoea, Afebrile, and Fat malabsorption leading to fatty stools. May resolve itself or become Chronic.</p> <p>Diagnosis:</p> <ol style="list-style-type: none"> Stool Exam: shows Cysts or trophozoites in stools String test, as giardia adheres to Duodenal surface. ELISA / antigen detection in stool <p>Treatment with Metronidazole</p>
Cryptosporidium Parvum /Hominis	<p>Transmitted via ingestion of Cyst in contaminated water.</p> <p>Causes Watery diarrhoea in AIDS / immunocompromised patients</p> <p>Diagnosed by demonstration of Oocysts in Stool. Oocyst is acid fast i.e., stained by ZN staining.</p> <p>Nitazoxanide – DOC</p>
Trichomonas Vaginalis	<ul style="list-style-type: none"> Only trophozoite form exists, no cyst form, flagellated, Pear shaped organism Transmitted via Sexual activity. 2nd common cause of vaginitis after Candida (1st). Presents with thin Greenish Yellowish vaginal discharge & Strawberry cervix

	<ul style="list-style-type: none"> Diagnosed by PCR (gold standard), Culture or Wet Mount exam. (2nd best) Treated with Metronidazole. Also screen the partner.
Malaria	<ul style="list-style-type: none"> Transmitted from Bite of female Anopheles mosquito (vector) Plasmodium is the parasite. 5 common spp have been identified as: <ul style="list-style-type: none"> Plasmodium Falciparum, Pl Vivax, Pl Ovale, Pl Malariae, Pl. Knowlesi. Pl Knowlesi is the newly identified spp. Pl. vivax & Pl. ovale cause Recurrent disease because they become inactivated in Hypnozoite form Pl. vivax > Pl. ovale malaria is the most common malarial form in Pakistan Sporozoite is infective form for Humans while Gametocyte is infective for mosquito. Merozoites are released from Liver when Schizonts rupture. Pl. Malaria has longest pre-erythrocytic stage and longest incubation period Pl. Falciparum has shortest pre- erythrocytic stage and causes cerebral malaria. Species causing most deaths: Pl. Falciparum. Trophozoite (Gametocyte) of Pl. Falciparum is Ring /Crescent/ Banana shaped while Oval/round for Pl ovale. Schuffner dots: punctate pigmentation in RBCs present in Pl. Vivax / Ovale malaria. Definitive host for plasmodium is Mosquito whereas Man is intermediate host. Infant parasite rate is the most sensitive indicator of recent malarial transmission in a community Infant parasite rate is calculated for below 5 yrs. of age. <p><u>Clinical Features:</u></p> <ul style="list-style-type: none"> Fever: High grade, intermittent nature, with Rigor & chills. Headache, nausea, myalgias, hypoglycemia, anemia, leucopenia, Hepatosplenomegaly. Type of Anemia is Hemolytic anemia and Normocytic, Normochromic picture. Severe forms present with Black water fever i.e., Haemoglobinuria. Cerebral malaria: presents with fever, headache, photophobia, and meningeal irritation signs. If severely complicated can lead to death eventually Benign tertian malaria: Fever spikes after every 48 hrs Pl. Vivax / Ovale is involved Malignant tertian malaria: Fever spikes after every 48hrs: Pl. Falciparum is the cause. Benign Quatern malaria: Fever spiked after every 72hrs. Pl. malariae is involved Quotidian malaria: Daily fever spikes every 24hrs: Pl Knowlesi > Pl. Falciparum. <p><u>Diagnosis & Treatment:</u></p> <ul style="list-style-type: none">  Microscopic exam of blood films i.e., Peripheral Smear using Giemsa stain. Thick and thin films are used. Thick films for Parasite identification. Thin films for plasmodial species identification  Rapid diagnostic tests e.g., immunochromatography/ Optimal test (detects LDH) help in spp identification.  Nucleic acid amplification test / PCR <ul style="list-style-type: none"> Primaquine is DOC for Hypnozoite form of Pl. vivax/ Ovale.it may cause G6PD anemia Chloroquine is DOC for Chloroquine sensitive falciparum malaria, Pl. vivax, Ovale & Pl. Malaria For chloroquine resistant malaria, Use Artemether- Lumefantrine For Falciparum related Cerebral malaria: use IV Artesunate. In pregnancy: Use Mefloquine for prophylaxis. Alternative -- Atovaquone/Proguanil (Fansidar) Chloroquine/ Doxycycline can be used for Chemoprophylaxis Chloroquine may cause Corneal Deposits, tinnitus, headache & GI upset.
Babesia Microti	<ul style="list-style-type: none"> A malaria like hemolytic illness transmitted by deer tick/ Ixodes tick Identified by Maltese Cross sign in the peripheral smear. Severe disease in Asplenic individuals. Treat with Azithromycin/ Atovaquone.
Leishmaniasis	<ul style="list-style-type: none"> A treatable and curable disease has following forms as given; 1. Cutaneous Leishmaniasis: caused by L. Tropical and Mexicans

	<ol style="list-style-type: none"> 2. Visceral Leishmaniasis/ Kala Azar: by L. donovani 3. Mucocutaneous Leishmaniasis: by L. Brazilians <ul style="list-style-type: none"> • Transmitted by Bite of Sand fly. • In Pak: common in Baluchistan, KPK and tribal areas. • Presents with Fever with rigors, Hepatosplenomegaly, and weight loss. • Skin ulcer can be present at bite site e.g., cheeks or Hands etc. <p>Diagnosed via</p> <ol style="list-style-type: none"> 1. PCR, Bone marrow / tissue aspiration 2. Microscopic demonstration of amastigotes (in macrophages) in blood films using Giemsa / Leishmania stain 3. Antigen / antibody detection tests <ul style="list-style-type: none"> • Treated with Amphotericin B (liposomal form) is DOC for Visceral form i.e., Kala Azar • Sodium Stibogluconate can also be used.
Trypanosoma Cruzi	<p>Chagas Disease/American Trypanosomiasis C for Chagas and Cruzi)</p> <ul style="list-style-type: none"> • Transmitted by bite of Reduviid bug (kissing bug). Bites on face while sleeping. • In acute form: Presents with lesion on Face + eye lid swelling (Romana's sign), fever, Lymphadenopathy, and weight loss. • In Chronic form: <ol style="list-style-type: none"> 1. GIT: Megaoesophagus & Megacolon 2. Cardiac: Cardiomyopathy, syncope, bradycardia, and Heart failure. 3. Neurological: Sensory impairment, dementia & altered tendon reflexes. • Diagnosed by: <ol style="list-style-type: none"> 1. microscopic exam (Peripheral smear showing Trypomastigotes) 2. Antigen/ antibody detection & PCR is also helpful. <p>Treat with Nifurtimox and benznidazole (1st line)</p>
Trypanosoma Brucei	<p>African Sleeping Sickness</p> <ul style="list-style-type: none"> • Transmitted via Tsetse fly (Vector) • Causes African sleeping sickness disease that presents with Fever, Somnolence, drowsiness. • Diagnosed via Trypomastigotes in Blood smear. • Treat with Suramin for blood related disease, Melarsoprol for CNS disease.
Toxoplasma Gondii	<ul style="list-style-type: none"> • Transmitted by Cysts in Meat / Oocysts in cat faeces. Also crosses placenta • Congenital toxoplasmosis: Hydrocephalus + Chorioretinitis + intracranial calcifications • In AIDS pts / immunocompromised hosts: Multiple Space occupying brain lesions Seen on MRI. • In immunocompetent hosts: Fever, flu, sore throat i.e., mononucleosis like illness but -ve heterophile Ab • Biopsy shows Tachyzoites in tissue. Serology & PCR also aid in diagnosis • Prophylaxis with Septran (TMP-SMZ) when CD < 100 cells/mm³. • Treat with Sulfadiazine + Pyrimethamine
Naegleria Fowleri	<ul style="list-style-type: none"> • Transmission is by Swimming in freshwaters and enters via cribriform plate from nose. • Causes rapidly progressive meningoencephalitis that is fatal -- also called Brain eating amoeba. • CSF exam may show amoeba and Amphotericin B is effective for some pts.

TREMATODES (FLUKES)

Schistosoma Spp. (Blood Flukes)	▪ Snails are intermediate host. Transmitted by penetration of Cercaria Larval in the skin.	
	Schistosoma Hematobium	<ul style="list-style-type: none">▪ Eggs with Terminal Spine. causes granulomatous disease & Squamous Cell carcinoma of bladder (painless hematuria)▪ Also associated with Pulmonary hypertension.▪ DOC --- Praziquantel
	Schistosoma Mansoni	<ul style="list-style-type: none">▪ Eggs with Lateral spine. Causes Portal hypertension by residing in portal vein. Congestive splenomegaly may be present
	Schistosoma Japonicum	<ul style="list-style-type: none">• Eggs with vague spines on sides.• Resides in Mesenteric veins. May cause CNS disease.
Clonorchis Sinensis (Liver Fluke)	▪ Transmitted by Undercooked fish leading to pigmented gall stones , biliary tree inflammation and even cholangiocarcinoma . Treated with Praziquantel	

CESTODES (TAPE WORMS)

Taenia Spp.	Taenia Solium (Pork Tapeworm)	<ul style="list-style-type: none"> Transmitted by larval ingestion in Undercooked Meat (Pork*) Causes Taeniasis (GI symptoms of indigestion, bloating) and Neurocysticercosis Neurocysticercosis: caused by ingestion of eggs in contaminated food (with faeces) On MRI: Racemose cysts may be seen in subarachnoid space / cisterns of brain Treatment: Praziquantel > Albendazole > Niclosamide. Albendazole prefer for CNS disease.
	Taenia Saginata (Beef Tapeworm)	<ul style="list-style-type: none"> Doesn't cause CNS disease. Transmitted by Larval ingestion in undercooked Beef. Causes GIT symptoms -- bloating, indigestion, nausea, abdominal pain. Treated with Praziquantel > Albendazole
Diphyllobothrium Latum (Fish tapeworm)	<ul style="list-style-type: none"> Transmission by Ingesting larvae in freshwater fish. Snail are intermediate host. May cause Vit B12 def anemia. Treated with Praziquantel > Niclosamide. 	

NEMATODES			
Worm	Transmission	Clinical Features	Diagnosis + Treatment
Enterobius vermicularis (Pin worm)	Feco-oral- eggs ingestion	Perianal itching especially at night as female lays eggs.	Diagnosed via Scotch tape test. Treat with Mebendazole.
Ascaris lumbricoides (Giant roundworm)	Feco-oral- eggs ingestion	Abdominal pain, gut obstruction, acute appendicitis may be triggered. Asthma by migrating to lungs.	Knobby-coated oval eggs in faeces. Treatment of choice: Mebendazole
Ancylostoma duodenale or Necator Americans (Hook worms)	larval penetration of skin while walking barefooted	Microcytic anemia Iron def anemia. Ground itch/ Serpiginous rash i.e., Cutaneous Larva migrans.	larvae seen in faeces under microscope. Treat with Mebendazole / Pyrantel pamoate.
Strongyloides stercoralis (Thread worm)	larvae penetrating skin. autoinfection - possible.	GI symptoms: duodenitis Pulmonary: Cough, hemoptysis Cutaneous: itching Hyper infection syndrome	Rhabditiform larvae seen in faeces under microscope. Treat with Ivermectin/Mebendazole
Trichuris trichiura (Whip worm)	feco-oral route	Loose stools. Rectal prolapse in children.	Albendazole - DOC
Trichinella spiralis	undercooked pork meat feco-oral (less likely)	Myalgias / myositis Peri-orbital edema, fever, vomiting	Albendazole / Mebendazole
Onchocerca volvulus	bite of female black fly	River Blindness Skin nodules + loose skin	Ivermectin
Loa loa	Bite of deer / horse / mango fly	Worm in conjunctiva Skin edema / swelling	Diethylcarbamazine
Wuchereria bancrofti (Brugia malayi)	bite of female culex mosquito	Symptoms occur after multiple infections over 1 yr. Elephantiasis (Lymphatic Filariasis)	Diethylcarbamazine
Drancunculus madinensis (guinea worm disease)	contaminated water with cyclops	Fever, urticaria, swelling, Dyspnea, and diarrhea etc.	No drugs available. Extraction of worm by stick / gauze.
Toxocara canis	feco oral	Visceral Larva Migrans e.g (inflammation of Liver, heart, CNS)	Albendazole

SCABIES	PEDICULUS HUMANUS /PHTHIRUS PUBIS
<ul style="list-style-type: none"> • <i>Sarcoptes scabiei</i>, (an ectoparasite) that is transmitted via Skin-to-skin contact (most commonly) or fomites • Mites burrow into Stratum corneum and type IV hypersensitivity reaction to (Mites Faeces > mites' eggs) causes intense itching that is worse at night and serpiginous lines b/w fingers and toes • Genital exam must be done to look for scratch marks / excoriations. • Treatment with 1% Permethrin cream and calamine lotion (for itching). Close contacts must be treated, and all bedding/ clothes must be washed and dried. • One version of scabies is Norwegian scabies especially in HIV +ve individuals. May be treated with Ivermectin. • Antibiotics may be used for secondary bacterial infection. 	<ul style="list-style-type: none"> • A Lice that sucks blood and causes pruritis commonly on Scalp & neck, axilla, waistband, and pubis. • Children with head lice can be treated at home without interrupting school attendance • Treat lice infestation with nit combing, Malathion or ivermectin lotion. • 5 % Permethrin can be used. (Remember that 1% Permethrin for Scabies) <p>Body Lice</p> <p>It can transmit following infections:</p> <ol style="list-style-type: none"> 1. Epidemic typhus: <i>Rickettsia prowazekii</i> 2. Trench fever: <i>Bartonella Quintana</i>. 3. Relapsing fever: <i>Borrelia recurrentis</i>.

MYCOLOGY

- Fungi are eukaryotic organisms having chitin in cell wall and exist in 2 forms (Yeast/Mold)
- Staining of fungi – with methenamine silver stain/ mucicarmine.
- Fungi can be Cultured on Sabouraud agar media .
- Resistance to echinocandin drugs : Cryptococcus > Candida albicans

Cutaneous Mycosis	<ul style="list-style-type: none">• Dermatophytes Includes Microsporum, Trichophyton, Epidermophyton.• Clinical features -- skin infections + Pruritis.• Branching septate hyphae have different shapes of conidia• Visible on KOH preparations with blue fungal stain. Treated with Terbinafine <p><u>Tinea Spp.</u></p> <p>T. capitis: on scalp. T. corporis: on torso / body. T. Cruris: inguinal area (Jock itch)</p> <p>T. pedis: Athlete’s foot. Interdigital . T. Ungulum: on Nails, Onychomycosis</p> <p><u>Clinical features</u></p> <ul style="list-style-type: none">• Erythematous enlarged scaly rings with central clearing especially in T. corporis• Jock itch doesn’t show central clearing• Alopecia, Lymphadenopathy, and scaling in T. Capitis• Diagnosis -- Wood lamp Exam can be used for dermatophytes.• Treat with Terbinafine, Ketoconazole etc. <p><u>Tinea Versicolor / Pityriasis</u></p> <ul style="list-style-type: none">• Not a dermatophyte. Caused by Malassezia spp. Commonly in hot humid conditions.• Less pruritic hypopigmented, hyperpigmented or pink patches.• Spaghetti & Meatball appearance of Yeast. Use Selenium sulphide/Topical or oral anti-fungal																					
Systemic Mycosis	<ul style="list-style-type: none">• All are dimorphic fungus i.e., Yeast (at 37C°), while Mold (at 20C°) except Coccidioides (Spherules)• All can cause Pneumoniae & disseminated disease. Can form granulomas like Tb• Can’t be transmitted from person-to-person contact. History & epidemiology helps in diagnosis• Treated with Amphotericin B for systemic inf and itraconazole/fluconazole for local. <table><tr><th>Fungi</th><th>Characteristic + Clinical Features</th><th>Diagnosis & Rx</th></tr><tr><td>Histoplasmosis</td><td>Associated with bird or bat drooping’s Macrophages filled with Histoplasma. Forms Cavitary lung lesions. Splenomegaly, erythema nodosum infects Reticuloendothelial system.</td><td>Common in Mississippi /Ohio Tongue Ulcer + caseating granuloma. Hilar lymph sign normal on CXR Diagnose by Urine/Serum antigen.</td></tr><tr><td>Blastomycosis</td><td>Inflammatory lung disease can disseminate to bones</td><td>Broad base budding Yeast. B for Broad & Blastomyces</td></tr><tr><td>Coccidioidomycosis</td><td>Exists in Spherule form filled with endospores Disseminates to bone/skin, erythema nodosum/multiforme, Arthralgias</td><td>Associated with Dust exposure e.g., Earthquakes/archaeological excavations</td></tr><tr><td>Para Coccidioidomycosis</td><td>Male > females. same features as blastomycosis</td><td>Budding yeast with captain’s wheel formation</td></tr><tr><td>Pneumocystis Jerevecii</td><td>Diffuse interstitial pneumonia + bilateral ground glass opacities start TMP-SMX when CD < 200 cells/mm3</td><td>Bronchoalveolar lavage or Biopsy shows disc/Boat shaped Yeast.</td></tr><tr><td>Sporothrix Schenkii</td><td>Rose Gardner’s disease/Sporotrichosis Ulcer with Nodules draining Lymphatics seen in farmers especially while pricked by a thorn</td><td>Cigar - shaped Yeast. Give Itraconazole / potassium iodide</td></tr></table>	Fungi	Characteristic + Clinical Features	Diagnosis & Rx	Histoplasmosis	Associated with bird or bat drooping’s Macrophages filled with Histoplasma. Forms Cavitary lung lesions. Splenomegaly, erythema nodosum infects Reticuloendothelial system.	Common in Mississippi /Ohio Tongue Ulcer + caseating granuloma. Hilar lymph sign normal on CXR Diagnose by Urine/Serum antigen.	Blastomycosis	Inflammatory lung disease can disseminate to bones	Broad base budding Yeast. B for Broad & Blastomyces	Coccidioidomycosis	Exists in Spherule form filled with endospores Disseminates to bone/skin, erythema nodosum/multiforme, Arthralgias	Associated with Dust exposure e.g., Earthquakes /archaeological excavations	Para Coccidioidomycosis	Male > females. same features as blastomycosis	Budding yeast with captain’s wheel formation	Pneumocystis Jerevecii	Diffuse interstitial pneumonia + bilateral ground glass opacities start TMP-SMX when CD < 200 cells/mm3	Bronchoalveolar lavage or Biopsy shows disc/Boat shaped Yeast.	Sporothrix Schenkii	Rose Gardner’s disease/Sporotrichosis Ulcer with Nodules draining Lymphatics seen in farmers especially while pricked by a thorn	Cigar - shaped Yeast. Give Itraconazole / potassium iodide
Fungi	Characteristic + Clinical Features	Diagnosis & Rx																				
Histoplasmosis	Associated with bird or bat drooping’s Macrophages filled with Histoplasma. Forms Cavitary lung lesions. Splenomegaly, erythema nodosum infects Reticuloendothelial system.	Common in Mississippi /Ohio Tongue Ulcer + caseating granuloma. Hilar lymph sign normal on CXR Diagnose by Urine/Serum antigen.																				
Blastomycosis	Inflammatory lung disease can disseminate to bones	Broad base budding Yeast. B for Broad & Blastomyces																				
Coccidioidomycosis	Exists in Spherule form filled with endospores Disseminates to bone/skin, erythema nodosum/multiforme, Arthralgias	Associated with Dust exposure e.g., Earthquakes /archaeological excavations																				
Para Coccidioidomycosis	Male > females. same features as blastomycosis	Budding yeast with captain’s wheel formation																				
Pneumocystis Jerevecii	Diffuse interstitial pneumonia + bilateral ground glass opacities start TMP-SMX when CD < 200 cells/mm3	Bronchoalveolar lavage or Biopsy shows disc/Boat shaped Yeast.																				
Sporothrix Schenkii	Rose Gardner’s disease/Sporotrichosis Ulcer with Nodules draining Lymphatics seen in farmers especially while pricked by a thorn	Cigar - shaped Yeast. Give Itraconazole / potassium iodide																				

Opportunistic Fungi	Four main clinically important opportunistic fungi are : Candida, Aspergillus, Cryptococcus, Mucor and Rhizopus		
	Fungi	Characteristic + Clinical Features	Diagnosis
	Candida albicans	<ul style="list-style-type: none"> • Dimorphic fungus: Forms germ tubes at 37C°, Pseudohyphae & budding yeast at 20C° • MCC of infection in 2nd /3rd trimester of pregnancy. • Oral and esophageal Thrush • Vulvovaginitis, Diaper Rash • Endocarditis • Inf is more likely in Immunocompromised, on Steroids, AIDS, antibiotics, Diabetics. • Thrush =Chronic Hyperplastic candidiasis • Vaginal discharge is thick, curdy, white - cottage cheese type 	<ul style="list-style-type: none"> • Pseudohyphae present. • Sabauroud's agar culture. • Fluconazole is DOC • Nystatin for oral thrush. Amphotericin B is for systemic /esophageal disease. • Resistance to Echinocandins is seen
	Aspergillus fumigates	<ul style="list-style-type: none"> • Catalase +ve • Produces Aflatoxin (HCC) • Infection More in Farmers • Forms granulomas in Lungs & fungus ball in already existing lung cavities. • Invasive aspergillosis in those with Chronic granulomatous disease • Aspergilloma (fungus ball) in TB pts having preexisting lung cavities • Allergic bronchopulmonary aspergillosis (asthma, eosinophilia, and bronchiectasis). 	<ul style="list-style-type: none"> • Septate hyphae branch at Acute angle -- associated with Rhinosinusitis • Give Voriconazole or echinocandins
	Cryptococcus neoformans	<ul style="list-style-type: none"> • Acquired through inhalation • Encapsulated. Non-dimorphic • Narrow-budding yeast • Resistant to Echinocandins • Found in Soil, pigeon drooping's • Meningitis/Encephalitis in HIV / immunocompromised patients. • Soap bubble lesions in Brain 	<ul style="list-style-type: none"> • India ink (clear halo) • mucicarmine (red inner capsule) • Latex agglutination test is more sensitive & specific. • Amphotericin B • Flucytosine, Fluconazole
	Mucor & Rhizopus	<ul style="list-style-type: none"> • Transmitted by spore inhalation • Proliferate in blood vessels endothelium • Penetrates Cribriform plate and invades Lamina paparyacea. • Mucormycosis in DKA, neutropenic and COVID patients on Steroids. • May cause rhinosinusitis, Headache, facial pain, cranial nerve palsies and cerebral thrombosis related death. 	<ul style="list-style-type: none"> • Non -septate hyphae branch at wide angle • Surgical debridement • Amphotericin B • Isavuconazole

VIROLOGY

- Viruses are considered b/w Living & Non – Living, have either DNA or RNA as genetic material and capsid made of Protein coat.
- They are classified according to Genetic material (DNA/RNA), Shapes (round, icosahedral etc), enveloped or non – enveloped (naked). Exchange of genetic material takes place as follows:

Reassortment	Exchange of genetic material b/w viruses having Segmented genomes . May cause Antigenic Shifts. Remember like, S in Reassortment, Segmented and Shift. E.g., SWINE FLU (H1N1), Avian Flu (H5N1)
Recombination	Exchange of genes by Crossing over . (C in recombination & crossing over)
Phenotype Mixing	Simultaneous infection of a cell by 2 viruses forms a hybrid virus . The infectivity of that hybrid virus depends upon the virus providing the protein coat for the hybrid virus.
Complementation	When 1 of 2 viruses that infect a cell has a mutation that results in non-functional protein, the non-mutated virus serves the mutated one by making a functional protein that serves both of them e.g., Hep B virus makes HbsAg that complements both Hep B & Hep D virus by providing envelope for Hep D

Summary Of Viral Genomes & Viral Envelope

- All DNA viruses are having double stranded DNA except Parvo virus which has ssDNA, and all RNA viruses have ssRNA except Reoviruses which have dsRNA.
- All DNA viruses have LINEAR genomes except PPH (Polyoma, papilloma and hepadnavirus) and All RNA viruses have Linear genomes except ABD (Arena viruses, Bunya viruses, Delta viruses) have circular/round.
- All DNA viruses are ENVELOPED except PAPP (Polyoma, adeno, Papilloma and Parvo viruses). You get naked for Pap smear
- All RNA viruses are Enveloped except CPR-h (Caliciviruses, Picorna viruses, Reoviruses, Hep viruses)
You do CPR of human to revive
- All DNA viruses have Icosahedral capsid except Pox virus (Complex). All RNA viruses have icosahedral capsids Except a few Helical
- Remember it like: A HELYX =** Arena, Rhabdo, Emperor (Corona), Filo + delta, Bunyavirus, Paramyxo viruses & Orthomyxovirus
A HELYX also applies at -ve stranded RNA viruses
- DNA Herpes viruses acquire envelop from nuclear membrane, rest all DNA viruses acquire from cell membrane
- Negative viruses and dsRNA viruses require Polymerase to become infection.

DNA VIRUSES

DNA viruses are **HHAPPPPy** viruses → Hepadeno, Herpes, Adeno, Pox, Parvo, Polyoma, Papilloma Viruses

HERPES VIRUSES (Enveloped, Linear, dsDNA)

- Include HSV-1, HSV-2, Varicella, CMV, EBV, HHV-6,7, HHV-8
- PCR/serology is the test of choice. Tzanck smear is obsolete now.
- Cowdry A inclusions seen in HSV-1/HSV-2 or VZV

Herpes Simplex Viruses	Herpes Simplex Virus -1 (HSV-1)	Herpes Simplex Virus-2 (HSV-2)
	<ul style="list-style-type: none"> Transmitted by Respiratory secretions/ saliva Causes: Herpes Labialis, keratoconjunctivitis, Temporal lobe encephalitis, esophagitis. MCC of Sporadic encephalitis. 	<ul style="list-style-type: none"> Transmitted via Sexual contact Causes neonatal herpes, painful genital lesions, vulval papules Viral meningitis → HSV-2 > HSV-1. Becomes latent in Sacral ganglia

	<ul style="list-style-type: none"> ○ Becomes Latent in Trigeminal Ganglia. ○ Activated by: Stress, Cold and immunosuppression etc. 	
Varicella Zoster Virus	<ul style="list-style-type: none"> • Transmitted by Respiratory secretions/contact of vesicular fluid, • Causes Chickenpox / Shingles. itchy Rash starts from trunk and spreads outward. Complications in adults include Pneumonia and encephalitis. • Becomes latent in Dorsal root ganglia / trigeminal ganglia. • MC complication of shingles is post-Herpetic neuralgia • Shingles involves dermatomal pattern-- commonly affected is CN V1 (Ophthalmic nerve) • Use Acyclovir for infection in adults. • Isolation and symptomatic treatment for majority of cases 	
Cytomegalovirus (CMV)	<ul style="list-style-type: none"> ❖ Transmission via saliva, Urine, sexual contact, Transplacental, transfusion. ❖ Most common and lethal virus in blood transfusion related infection is CMV. ❖ Infected cells have OWL Eye intranuclear inclusions. Becomes latent in Mononuclear cells. ❖ CMV retinitis (with Cotton wool exudates) is indicative of AIDS. ❖ It may cause Mononucleosis like illness i.e., fever, sore throat, hepatosplenomegaly but negative Monospot test. ❖ CMV can also lead to diarrhoea, pneumonia, and esophagitis 	
Ebstein Barr Virus (EBV)	<ul style="list-style-type: none"> 🚫 No Vaccine available for EBV 🚫 aka kissing disease, common in teenagers transmitted via saliva / Respiratory secretions. 🚫 causes infectious mononucleosis (Fever, sore throat, risk of Splenic rupture), Hodgkin lymphoma, nasopharyngeal carcinoma, Burkitt lymphoma, Post-transplant Lymphoproliferative disorder. 🚫 use of Amoxicillin may cause Maculopapular rash 🚫 Infects B cells but activated cells are Cytotoxic T cells. 🚫 Atypical lymphocytosis on blood smear. Positive Monospot test or Paul Bunnell test 	
Human Herpes Viruses	<ul style="list-style-type: none"> • HHV 6 & 7: transmission via saliva, causes Roseola infantum. (HHV-6 > HHV-7). • HHV- 8: Sexual contact transmits HHV-8, causes Kaposi sarcomas in AIDS / immunosuppressed/ transplant pts. Kaposi sarcoma is common on Head & neck region consists of Dark purple / violaceous plaques or nodules. 	

SUMMARY OF OTHER DNA VIRUSES

- ❖ Pox virus is largest DNA virus, may cause smallpox and Cow pox and Parvo virus is the smallest DNA virus that can cause slapped cheeked syndrome (5th disease), aplastic crisis, Hydrops fetalis and arthritis.
- ❖ Molluscum contagiosum infection is characterized by flesh colored Umbilicated papules.
- ❖ Hepadnavirus includes HBV, has partially ds DNA, circular & has reverse transcriptase as well.
- ❖ Adenovirus vaccine is given to military recruits, virus may cause fever, Conjunctivitis (Pink Eye), myocarditis.
- ❖ HPV: HPV serotypes 1,2,6,11 causes Warts and serotypes HPV 16,18 causes Cancer.
- ❖ Polyoma viruses include JC & BK viruses.
 - BK = Bad Kidney. MCC of infection in Kidney transplant patients*
 - JC Virus causes Progressive Multifocal leukoencephalopathy (PML) in HIV
 Keep in Mind that.
 - ✓ Condyloma acuminatum is caused by HPV.
 - ✓ Condyloma lata is present in secondary Syphilis

RNA VIRUSES

1. **Picorna Viruses:** Hep A, Polio, Rhino, echo, Cocksackie virus
 - ✓ Echo virus may cause Meningoencephalitis.
 - ✓ Cocksackie virus is most common cause of Myocarditis and also causes Hand, foot & mouth disease.
 - ✓ Rhino viruses cause common Cold / flu.
2. **Reo Viruses:** 10-12 segmented virus.
 Reo biscuit is 2 layered. So reoviruses are double stranded RNA viruses. Most imp one is ROTA.
 - Rota virus may cause Acute watery fatal diarrhoea in infants and children. it may resolve itself.
 - Most imp global cause of infant viral gastroenteritis.
 - Rota vaccine is a Live Oral Vaccine, contraindicated in Intussusception.
3. **Hepe Virus** = Hep E virus.
4. **Calicivirus** = Noro virus (causes Gastroenteritis)
5. **Flavi Viruses:** Hep C, Dengue, Yellow Fever, ZIKA Virus, West Nile virus
6. **Toga Viruses:** Rubella, Chikungunya
7. **Retro Viruses:** HIV, HTLV
8. **Corona Viruses:** enveloped, single stranded + ve, linear, Helical
9. **Orthomyxoviruses:** 8 segments, Influenza virus
10. **Paramyxo Viruses:** Measles, Mumps, Parainfluenza, Respiratory Syncytial virus. Note that M, R, P in Paramyxo.
 All Paramyxo viruses are Nonsegmental and contain F (fusion) proteins.
11. **Rhabdo Viruses:** Rabies virus
12. **Filo Viruses:** Ebola virus
13. **Arena Virus:** 2 segments, may cause Lassa fever encephalitis.
14. **Bunya Virus:** Crimean Congo virus, Hanta virus, Rift valley fever.
15. **Delta Virus:** Hep D

RESPIRATORY RNA VIRUSES

Influenza virus (Orthomyxovirus)	<ul style="list-style-type: none"> ○ Contains haemagglutinin /HA (for virion entry) and neuraminidase/NA (for virion release) ○ Mutation in HA / NA may cause Genetic drifts (minor change) whereas Reassortment leads to Genetic Shifts (Major changes). ○ Both Shifts and drifts may cause Global Outbreaks / Pandemics. But shift is more lethal ○ Causes Flu commonly and may progress to pneumoniae in old, debilitated pts with co-morbid. ○ S. Pneumoniae > S. Aureus super infection is seen with influenza infection. ○ Killed Vaccine is most commonly used, Live attenuated vacc. is administered intranasally. ○ Treatment with Oseltamivir (DOC) and supportive care.
Measles (Paramyxo Virus)	<ul style="list-style-type: none"> ○ Respiratory route. Triad of 3 Cs → Cough, Coryza and Conjunctivitis ○ Low grade Fever. Rash starts from face, behind ears towards trunk and abdomen ○ Koplik Spots in Buccal mucosa are pathognomonic but not always present. ○ Warthin Finkedley giant cell are present. Serology helps in diagnosis. ○ Vitamin A is helpful in treatment. Vacc is Live type given S/C ○ Complications -- Subacute sclerosing panencephalitis ○ Giant cell pneumonia-most common cause of measles related death in children ○ MC complication is acute Otitis media ○ Cough lasts longer than any other symptom.
Rubella (Toga virus)	<ul style="list-style-type: none"> ○ Aka as German measles - same rash as measles but posterior cervical lymphadenopathy is present. Blueberry muffin appearance. ○ If IgM Ab are present, Counsel the female not to conceive. ○ 2 doses Vaccine Must be given to all women in reproductive age ○ Complication -- Most Common and after 7 weeks is Deafness ○ Before 7 weeks Cataract. Cardiac like PDA in 5-10 weeks
Mumps (Paramyxo Virus)	<ul style="list-style-type: none"> ○ Respiratory route. Presents with Fever, bilateral cheek swelling, (Parotitis)

	<ul style="list-style-type: none"> Supportive care needed. Observe for complications Complications -- Orchitis -- May cause sterility. Pancreatitis, Oophoritis. Meningitis
Respiratory syncytial virus (Paramyxo Virus)	<ul style="list-style-type: none"> Respiratory route. RSV Causes cough, fever, and bronchiolitis. Supportive care required and may complicate to pneumoniae
Para influenza virus (Paramyxo Virus)	<ul style="list-style-type: none"> Respiratory route. Causes fever, cough, acute laryngotracheobronchitis (CROUP) Croup is diagnosed on X ray neck -- by Steeple sign Pavalizumab is helpful with supportive care. Complication -- pneumoniae
Corona virus	<ul style="list-style-type: none"> SARS-CoV-2 is a novel +ve ssRNA virus Spreads primarily through respiratory droplets and aerosols. Host cell entry occurs by attachment of viral spike Protein to ACE-2 receptor Clinical course varies; often asymptomatic. Symptoms include fever, dry cough, shortness of breath, fatigue. More specific: anosmia (loss of smell) dysgeusia (altered taste). Complications: respiratory failure, hypercoagulability, shock, organ failure, death. Risk factors for severe illness or death: increasing age, obesity, diabetes, hypertension. chronic kidney disease, and severe cardiopulmonary illness. Diagnosed by RT-PCR (most common); antigen and antibody tests are available. Treatment options for hospitalized adults include remdesivir (nucleoside analogue), convalescent plasma, and dexamethasone (to prevent Cytokine storm)

RNA VIRUSES TRANSMITED BY VECTORS

Dengue virus	<ul style="list-style-type: none"> Transmitted via mosquito -- Aedes Aegypti bite. Causes dengue fever Symptoms include High grade fever with rigor & chills, Retro orbital pain, backache, Myalgias Leucopenia, low Platelets, Low /very high Hct. Dengue shock syndrome is caused by infection with a different serotype of virus, present with hemorrhagic tendencies like Epistaxis, GI bleed, per rectal bleed etc. Mechanism of Dengue shock syndrome: Antibody dependant enhancement of disease due to previous infection with another serotype. Diagnosed by PCR / Serology. NS 1 Test is nonspecific. Supportive treatment, Monitor PLT. Live recombinant vaccine using yellow fever virus.
Yellow fever virus	<ul style="list-style-type: none"> Transmitted via Aedes mosquito bite. Human / Monkey reservoir Presents with Fever, Jaundice, black vomitus, myalgias, Headache. Councilman bodies on liver biopsy Following are cycles of transmission: Sylvatic / Enzo-otic cycle: B/w Monkeys and Mosquitos Rural / Epizo-otic cycle: B/w Human and Non-human primates' animals & Mosquito Urban cycle/Epidemic: B/w Human & Mosquito
Rabies virus (Bullet shaped)	<ul style="list-style-type: none"> Transmitted by dog bite in Asia commonly but from bat, raccoon & Skunk bites in USA, rabbits, Jackals, fowls may also be the source. Virus travels to CNS by migrating retrogradely (via dynein motors) after binding to Ach receptors. Presents with fever, malaise, agitation, Photophobia, Hydrophobia, hypersalivation, Coma and Death. Negri bodies may be found in Purkinji cells of cerebellum and in hippocampal neurons. Treat with Both killed Vaccine + human Immunoglobulins. i.e Post exposure prophylaxis
Chikungunya virus	<ul style="list-style-type: none"> Transmitted by Aedes mosquito. Systemic infection Produces: inflammatory polyarthritis that can become chronic. Other Symptoms include high fever. maculopapular rash, headache, lymphadenopathy Hemorrhagic manifestation uncommon. Diagnosed with RT-PCR / serology. No antiviral therapy/ vaccine.

Zika virus	<ul style="list-style-type: none"> Transmitted by Aedes mosquito. Causes conjunctivitis, low-grade pyrexia, and itchy rash. Sexual and vertical transmission occurs. Can lead to miscarriage or Congenital Zika syndrome: Brain imaging shows Ventriculomegaly, subcortical calcifications. Clinical features include Microcephaly, Ocular anomalies, and Motor abnormalities (spasticity, seizures) Diagnosed with RT-PCR / serology. Supportive Management only.
-------------------	---

Ebola virus	<ul style="list-style-type: none"> Transmission requires direct contact with bodily fluids, fomites (including dead bodies, infected Bats or primates. Presents with flu-like symptoms, diarrhoea, vomiting, high grade fever, myalgia. Can progress to DIC, diffuse Hemorrhage, and shock Diagnosed with RT-PCR within 48 hr of symptom onset. High mortality rate Supportive management only. Vaccination of contacts and isolation of infected individuals.
Congo virus	<ul style="list-style-type: none"> Transmitted by tick bite or contact with infected body fluids It causes Crimean-Congo hemorrhagic fever. Epidemics on Eid-ul-Azha from infected cattle Symptoms – fever, headache, hemorrhagic tendencies (epistaxis, ecchymosis, petechiae) Supportive treatment.

HEPATITIS VIRUSES

- Episodes of fever, jaundice, raised ALT and AST are common to All hepatitis viruses.
- Naked viruses (HAV & HEV) lack envelope and: are not destroyed by the gut.
- HBV DNA polymerase has DNA- and RNA-dependent activities
- HCV lacks 3'5' exonuclease activity -- no proofreading ability, antigenic variation of HCV envelope Proteins.

Host antibody production lags production of new mutants' strains of HCV

HAV	<ul style="list-style-type: none"> Feco-oral route (shellfish) common in Travellers, and day care centres Short incubation period (weeks). Acute and self-Limiting (in adults). Asymptomatic in children. Good prognosis On Biopsy -- Hepatocyte Swelling, Monocyte Infiltration, and Councilman Bodies. No carrier state. No HCC Risk. HAV diagnosed by IgM Ab to HAV.
HBV	<ul style="list-style-type: none"> Transmission via Parenteral (Blood). Sexual (Bedroom). Perinatal (Birthing). NOT Present in Stool. MC Hepatitis virus spread by Blood transfusion. Longest incubation period (6 weeks to 6 months) Presents: Initially like serum Sickness (fever, Arthralgias, rash) May cause HCC directly via HBx gene or indirectly via cirrhosis. Risk of HCC: Hep B > Hep C Mostly in Adults Full resolution may occur while in Neonates – worse Prognosis On Biopsy: Granular Eosinophilic Ground Glass Appearance due to accumulation of surface antigen Within infected Hepatocytes -- Cytotoxic T cells Mediate damage Carrier state Common. 90 % neonates become chronic carrier. Extrahepatic manifestations: Aplastic anemia, Membranous GN > membranoproliferative GN Polyarteritis nodosa association in 30 % cases
HCV	<ul style="list-style-type: none"> Primarily blood (IV drugs' abusers) Posttransfusion. Long incubation period May progress to Cirrhosis OR Carcinoma. Risk of Cirrhosis: Hep C > Hep B Majority develop Stable, Chronic Hepatitis C On Biopsy: Lymphoid Aggregates with Focal areas of Microvesicular Steatosis Carrier state very Common. Extra hepatic manifestations: include Essential mixed Cryoglobulinemia, Aplastic anemia, Porphyria Catenae Tarda, Lichen Planus, Membrano-Proliferative Glomerulonephritis, NHL, ITP, hemolytic anemia. Sofosbuvir and ribavirin are preferred Oral drugs. INTERFERON can be given IV.

HDV	<ul style="list-style-type: none"> • sexual Practices, Perinatal especially. • Superinfection HDV after HBV Has shorter incubation if Coinfection (With HBV) = longer incubation. • Superinfection has Worst prognosis causes. Disease Similar to HBV. • Defective virus. Depends On HBV For entry into Hepatocytes. Risk of HCC present • Presence of Delta Ag suggests Chronicity > Measure of Lethality.
HEV	<ul style="list-style-type: none"> • Fecal-oral, Especially Waterborne. Short incubational period. No. Carrier state and no risk of HCC. • Epidemic (in Asia & Africa). Fulminant hepatitis In Expectant (pregnant) Patients). High mortality in Pregnant patients • Patchy necrosis on Biopsy

KEY FACTS – HEPATITIS

- o Hep A & E both Naked viruses & spread by Feco – Oral route.
- o MC Hepatitis in Asia + in children as well is Hep A (Eating from sub-standard restaurants & Hotels).
- o Hep E causes Epidemics most commonly and is mainly water-borne.
- o Risk of HCC: Hep B+C > Hep B > Hep C
- o Hep B is MCC of HCC Worldwide, whereas in PAK: Hep C
- o Risk of Cirrhosis: Alcohol > Hep C > Hep B
- o Ground glass appearance of HbsAg in Hep B
- o PAN is associated with Hep B and Mixed Cryoglobulinemia + Lichen planus linked with hep C.
- o Hep E is Lethal in Pregnancy, highest mortality & Morbidity in pregnancy.
- o Chronic Carrier state (especially for neonates): Hep B > Hep C
- o Hep B usually resolves in adults in 90% cases.
- o MC Hep virus transmitted by Blood transfusion: HEP B > HEP C
- o Overall MC + Lethal via blood transfusion: CMV
- o Presence of delta antigen suggests: Chronicity > Measure of Lethality

HBsAg	ANTI-HBs	ANTI-HBc	HBeAg	ANTI-HBe	INTERPRETATION
+	-	IgM	+	-	Acute hepatitis B, high infectivity
+	-	IgG	+	-	Chronic hepatitis B, high infectivity
+	-	IgG	-	+	1. Late acute or chronic hepatitis B, low infectivity 2. HBeAg-negative ("precore-mutant") hepatitis B (chronic or, rarely, acute)
+	+	+	+/-	+/-	1. HBsAg of one subtype and heterotypic anti-HBs (common) 2. Process of seroconversion from HBsAg to anti-HBs (rare)
-	-	IgM	+/-	+/-	1. Acute hepatitis B ^a 2. Anti-HBc "window"
-	-	IgG	-	+/-	1. Low-level hepatitis B carrier 2. Hepatitis B in remote past
-	+	IgG	-	+/-	Recovery from hepatitis B
-	+	-	-	-	1. Immunization with HBsAg (after vaccination) 2. Hepatitis B in the remote past (?) 3. False-positive

HUMAN IMMUNO DEFICIENCY VIRUS (HIV-AIDS)

	<p>The 3 structural genes (protein coded for):</p> <ol style="list-style-type: none"> 1. Env (gp120 and gp41): gp120-attachment to host CD4 T cell. Gp41-fusion and entry. 2. Gag (p24 and p17)- Capsid and matrix Proteins, respectively 3. Pol-Reverse transcriptase – Integrase <p>Reverse transcriptase synthesizes dsDNA from Genomic RNA; dsDNA integrates into host Genome</p>
Receptors	<p>✚ Virus binds CD4 as well as a coreceptor, either CCR5 on macrophages (early infection) or CXCR4 on T cell (late infection)</p> <p>✚ Homozygous CCR5 mutation = immunity. Heterozygous CCR5 mutation = slower course.</p>
Transmission	<ul style="list-style-type: none"> ○ Via Par enteral (Blood & Blood products), Sex, Vertical (Transplacental) and Unsterilized Syringes/Needles. ○ Blood transfusion is Most Efficient route of HIV inf ○ while Sexual route is the Most common route for HIV inf. ○ HIV is NOT Transmitted through: Sweat, Tears, Saliva, kissing, hugging, sharing Utensils, air /droplet / Insect Bites.
Diagnosis of HIV	<p>✚ Most sensitive & initial test is ELISA (detects Viral p24 Ag capsid protein)</p> <p>✚ Confirmatory Test is Western Blot (Not done now a days and not done in children)</p> <p>✚ PCR: To detect Viral load and check Progression from Asymptomatic to Symptomatic disease.</p> <p>To diagnose in Child / Neonates use PCR.</p> <p>✚ CD4+Count: To monitor response to therapy.</p> <p>✚ HIV-1/2 Ag. Very high sensitivity/specificity</p>
Diagnosis of AIDS	<ol style="list-style-type: none"> 1. < 200 CD4+ cells/mm³ (normal: 500-1500 cells/mm³) or 2. HIV +ve with AIDS-defining condition (eg, Pneumocystis)
Stages of infection	<p>Four stages of untreated infection:</p> <ol style="list-style-type: none"> 1. Flu-like (acute): Fever, Flu, Sore throat, myalgias. 2 -4 weeks after exposure. 2. Feeling fine (latent): Asymptomatic stage. During latency virus resides in Lymph nodes. 3. Falling count: Chronic infection including fever +weight loss + fatigue + diarrhoea 4. Final crisis: AIDS defining illnesses & opportunistic infections. <ul style="list-style-type: none"> ➤ HALL MARK of HIV: Proliferation of virus inside T cells ➤ HALL MARK of AIDS: Progressive immunodeficiency
AIDS defining illnesses	<p>Following Are Aids Defining Diseases</p> <ul style="list-style-type: none"> • Esophageal candidiasis, CMV Retinitis, Pneumocystis Jerovecii, Kaposi Sarcoma, Cryptococcal pneumonia, Chronic diarrhoea (by atypical mycobacteria E.g., MAC, Cryptosporidium and CMV), and Primary CNS Lymphoma etc. • Mycobacterium avium Complex infection at CD4+ < 50 cells/mm³ (Prophylaxis with Azithromycin) • Toxoplasma gondii: CD4+ < 100 cells/mm³ • Pneumocystis pneumoniae: CD4+ < 200 Cells/mm³ • TB & bacterial Pneumonias: CD4+ < 500 Cells/mm³ • Non -Ring Enhancement Lesion on CT Brain: Progressive Multifocal Leukoencephalopathy (PML) • Single Ring Enhancement Lesion on CT Brain/ Single SOL Brain: Primary CNS Lymphoma • Multiple Ring Enhancement Lesions on CT Brain / Multiple SOL Brain: Toxoplasmosis • Regarding Needle Prick Injury: Risk of Transmission for HIV, Hep B and Hep C <ul style="list-style-type: none"> • Hep B (30 %) > Hep C (3 %) > HIV (0.3 %)
Treatment	<ul style="list-style-type: none"> ❖ Ante-retroviral therapy is started at the time of diagnosis especially in those having AIDS defining illness, declining CD4+ Counts < 200 cells/mm³ or high viral load. ❖ Standard regimen comprises of 2 NRTIs + 1 integrase inhibitors. ❖ Zidovudine Prophylaxis may be given in pregnancy and to prevent fetal transmission.

- ❖ Nucleoside reverse transcriptase inhibitor -- NRTIs: Abacavir, Tenofovir, Zidovudine (bone marrow suppression)
- ❖ Integrase inhibitors: Raltegravir, Dolutegravir (increase CK enzyme)
- ❖ NON-Nucleoside reverse Transcriptase inhibitors NNRTIs: Nevirapine, Efavirenz
- ❖ Protease inhibitors: Ritonavir, Lopinavir. (Cause -- Cushingoid features / Obesity)
- ❖ Entry inhibitors: Enfuvirtide, Maraviroc.

Frequently Asked Questions Regarding Opportunistic Infections

- MC Opportunistic infection in HIV: T.B While in AIDS: Pneumocystis Jerovecii/ carinii (ground glass appearance.)
- MC Opportunistic Fungal infection in HIV/AIDS: Candida Albicans.
- MC Opportunistic Fungal meningitis in HIV: Cryptococcus (India ink + Clear Halo)
- Oral thrush is scrapable White Plaque whereas Hairy Leukoplakia is Unscrapable white Plaque on lateral tongue caused by EBV in HIV. Hairy Leukoplakia may be caused by Growth of Chemogenic bacteria.
- Abdominal Mass in HIV Patient: B cell – NHL.
- Kaposi Sarcoma caused by HH8 Virus in AIDS, most common on Head & Neck and findings include purple lesions consisting of Dilated Endothelial channels and Perivascular Spindle Cells (details are given in CVS).

MISCELLANEOUS TOPICS

Stain	Organisms
Giemsa	Plasmodium, Chlamydia, Rickettsia, H. Pylori and Trypanosomes
Silver	Pneumocystis, H. Pylori, Legionella
Periodic acid Schiff	Entamoeba, Tropheryma whipplei (Whipple disease) PAS also stains Glycogen.
India ink	Cryptococcus neoformans
Fluorescent antibody	Giardia, Cryptosporidium many viruses + bacteria

- Gram Stains (1st line lab test in bacterial inf) & ZN Stain have been described in bacteriology portion above.
- Auramine-Rhodamine stain is preferred than ZN stain (Carbol Fuchsin) now due to high sensitivity and inexpensive also

SPECIAL CULTURE REQUIREMENTS

MEDIA	ORGANISMS
Subauroud agar	Subauroud for Fungi
L J Agar, Middle Brook Medium (Liquid. Media for TB)	
Chocolate agar (Contains factor V (NAD+) and Factor X (hematin))	H. influenza
MacConkey agar	Lactose-fermenters. E.g., E. coli , Klebsiella, Enterobacter.
Eaton agar	M. Pneumoniae
Eosin Methylene blue agar	E. Coli forms colonies with green metallic sheen.
Charcoal Yeast agar extract Buffered with Cysteine & Iron	All with <u>ella</u> s i.e., Brucella, legionella, Francisella, Pasteurella
Tellurite agar, Löffler Medium	C. Diphtheriae
Bordet-Gangou agar	Bordetella pertussis
Thayer -Martin agar (contains Vancomycin, Colistin, Nystatin and Trimethoprim)	Neisseria spp (gonorrhoeae, Meningitidis)

Encapsulated Organism Capsule is antiphagocytic and gives virulence	<ul style="list-style-type: none"> ➤ <i>S. pneumoniae</i> ➤ <i>Pseudomonas</i> ➤ <i>Klebsiella</i> – thick mucoid capsule. ➤ <i>E. Coli</i> ➤ <i>Salmonella</i> ➤ Group B streptococcus ➤ H Influenza b. ➤ <i>Cryptococcus</i> – thick capsule, stains with India ink
Urease +Ve Organisms	<ul style="list-style-type: none"> ➤ <i>Proteus</i>, <i>H. Pylori</i>, <i>Klebsiella</i>, ➤ <i>staph. Epidermidis</i>, <i>Stap saprophyticus</i> ➤ <i>Cryptococcus</i>
Catalase +Ve Organisms	<ul style="list-style-type: none"> ➤ <i>Candida</i>, <i>Aspergillus</i> ➤ <i>Staph aureus</i>, <i>Staph Epidermidis</i> ➤ <i>E. Coli</i>, <i>H. Pylori</i>, <i>Pseudomonas</i>, ➤ <i>Listeria</i>, <i>E. Coli</i> and <i>Nocardia</i>
Pigment Producing	<ul style="list-style-type: none"> ❖ <i>S. aureus</i> – Golden yellow colonies ❖ <i>Actinomyces Israeli</i>- yellow sulphur granules ❖ <i>Pseudomonas</i>: Green, blue, fruity grape like odour ❖ <i>Serratia</i>: Red Pigment
Spore Forming	<ul style="list-style-type: none"> ✓ <i>Bacillus</i> ✓ <i>Clostridium</i> spp.

STERILIZATION AND DISINFECTION

- ✓ Sterilization is killing of all forms of life & micro-organisms -- Including Endospores.
- ✓ Disinfection is killing of Organisms on inanimate objects or surfaces (Non-living things) while Antiseptics are applied on Skin.
- ✓ Linen (Gown, caps, mask, drapes) --- autoclaving
- ✓ Metal instrument----autoclaving. HEPA Filter uses 3 layers chambers.
- ✓ Plastic instruments/components----ethylene oxide sterilization, formalin chamber
- ✓ Sharp edges instrument-----ETO/hot air oven/chemical disinfection
- ✓ Alcohol-based hand hygiene product contains chlorhexidine gluconate, used for Disinfection of hand
- ✓ Spore killed by dry heat at 160 C for 2 hour or in autoclave heating at 121 .C for 15mins
- ✓ All samples for routine histology are immediately placed in fixative, usually formalin (10% formaldehyde) to preserve morphology and to prevent autolysis
- ✓ Heal labile Instruments by ETO
- ✓ Needles / Syringes -- Gamma sterilization
- ✓ Heating for 3 days, 1 hr daily, at 80C -- Inspissation
- ✓ Heating for 3 days, 1hr daily, 100C -- Tyndallisation
- ✓ Endoscopes sterilization by Tyndllization or 2% Glutaraldehyde
- ✓ To Clean Floor in HIV pt OT – use 1% Hypochlorite
- ✓ To Clean instruments in HIV case – use 2 % Glutaraldehyde
- ✓ Autoclaving uses Steam, 121° for 15 mins at 15ppi.
- ✓ Dry heat kills by Oxidation. Moist heat kills by Coagulation of Proteins
- ✓ Lypholization or freezing Cold may be used for sterilization
- ✓ 5%Isoprophyl alcohol may be used for Hand washing
- ✓ Humidity in OT -- 55% . OT cleaning -- Formaldehyde and sterilization with UV Radiations.
- ✓ Pasteurization of Milk decrease Vit-B & Vit C
- ✓ Washing of face mask with Lukewarm water. Sterilize face mask with Ethylene Oxide (ETO)
- ✓ Flash Pasteurization/ Hight Temp Short Time Pasteurisation (HTST) involves heating milk products / beverages at 72C for 15-20 sec. Batch / Vat / Low Temp Long Time (LTLT) Pasteurization: heating at 63C° for 30 mins.
- ✓ Ultra – high temp Pasteurization: heating at 138C for 2 seconds.
- ✓ Body fluids & Vaccines disinfection -- by Filtration.
- ✓ Thermometer and Stethoscope disinfection by Alcohol.
- ✓ **Autoclave principle:** Pressurized Steam at >120 C. Sporicidal. Denaturation +Protein coagulation.
- ✓ Bone graft and tissues are sterilized by radiations

- ✓ Prions are most resistant to antiseptics whereas lipophilic viruses are least resistant.
- ✓ Minimum Inhibitory Concentration: MIC is defined as the lowest concentration of antimicrobial or drug that will inhibit the visible growth of bacteria after overnight incubation
- ✓ Minimum Bactericidal Conc.: MBC is the lowest concentration of antibacterial agent required to kill a particular bacterium.
- ✓ Chlorine, ETO, H₂O₂, heat is Sporicidal and virucidal as well.
- ✓ Autoclave may not inactivate Prions.
- ✓ Frequent Hand washing may reduce the risk of infection in ICU settings
- ✓ High Level disinfection kills all Micro org. Except some bacterial spores
- ✓ Intermediate level disinfectants kill Mycobacterium, vegetative bacteria, most viruses, fungi but not Spores
- ✓ Low level disinfectants inactivate some bacteria, some viruses, and some fungi but not M. tuberculosis/Spores
- ✓ Prions & Endospores being Most Resistant to disinfections
- ✓ Spores contain: Dipicolinic acid, low water content, Ca⁺, and are resistant to Heat, dehydration & desiccation
- ✓ Dry Heat at 160° for 2 hr (sometimes 1hr mentioned, prefer 2 hr) & Moist heat at 121°C for 15 mins kills spores.
- ✓ Hospital waste is managed by Incineration mostly.

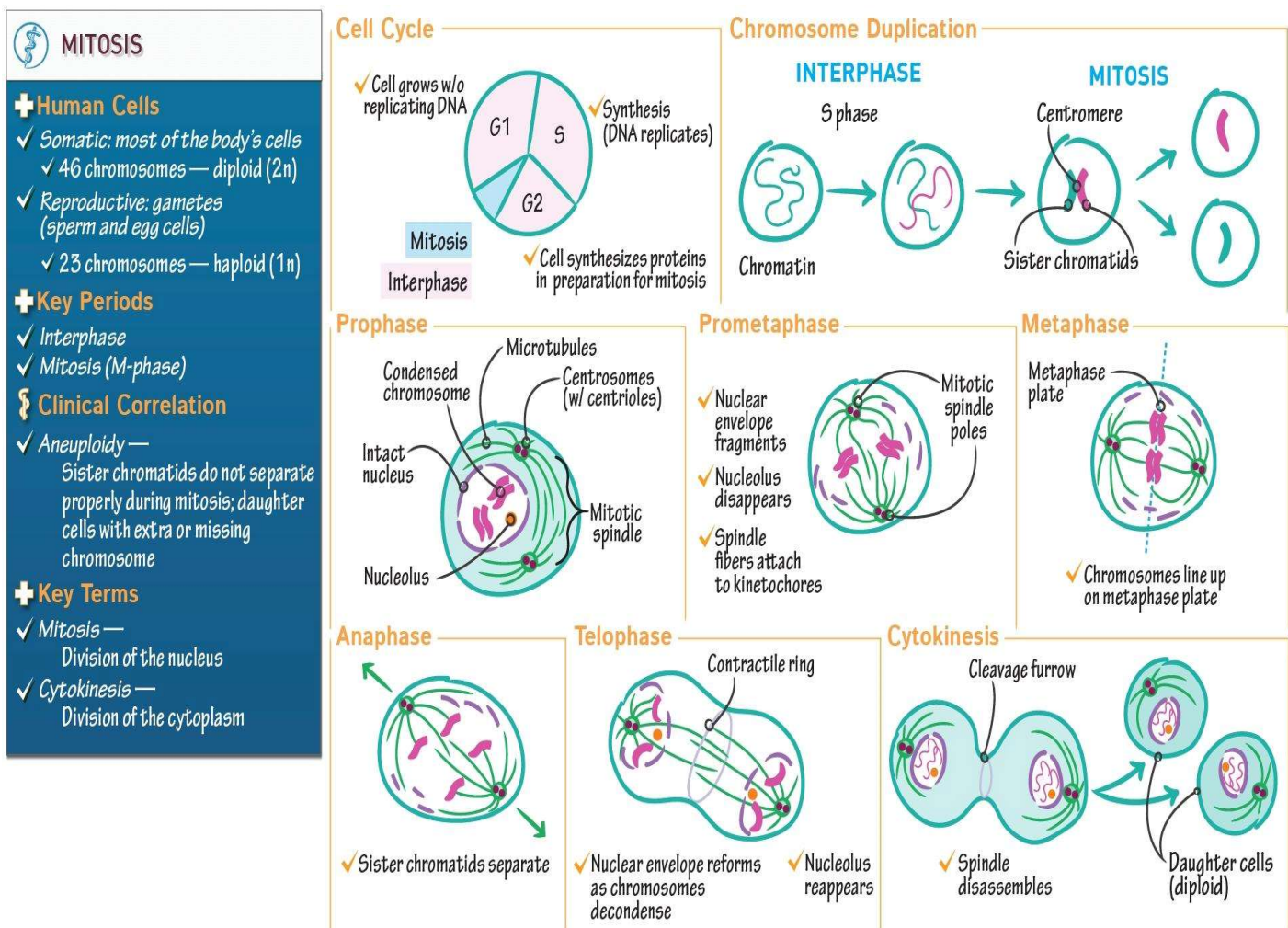
SHARPS Red Sharps Container <ul style="list-style-type: none"> ✓ Needles ✓ Ampules ✓ Broken Glass ✓ Blades ✓ Razors ✓ Staples ✓ Trocars ✓ Guide Wires ✓ Other Sharps 	BIOHAZARD Red Container or Red Liner in Container <ul style="list-style-type: none"> ✓ Infectious Waste ✓ Blood Products (albumin, etc.) ✓ Contaminated Personal Protective Equipment (PPE) ✓ IV Tubing ✓ Cultures, Stacks 	TRACE CHEMO Yellow Container <ul style="list-style-type: none"> ✓ Empty vials, ampules ✓ Empty Syringes, Needles ✓ Empty IVs ✓ Gowns ✓ Gloves ✓ Tubing ✓ Aprons ✓ Wipes ✓ Packaging 
RCRA HAZARD Black Container <ul style="list-style-type: none"> ✓ Hazardous meds (RCRA) ✓ Half/Partial doses (RCRA) ✓ Hazardous bulk meds ✓ P-listed drugs, packaging ✓ Bulk chemo ✓ Pathological Waste (Incineration Only) 	PHARMACEUTICAL Blue Container <ul style="list-style-type: none"> ✓ Pills ✓ Injectables ✓ Antibiotics 	RADIOACTIVE Shielded Containers with Radioactive Symbol <ul style="list-style-type: none"> ✓ Fluorine-18 (F-18). 110 minutes half-life. ✓ Technetium-99 (Tc-99m). 6 hours half-life. ✓ Iodine-131 (I-131). 8 days half-life. ✓ Strontium-89 (Sr-89). 52 days half-life. ✓ Iridium-192 (Ir-192). 74 days half-life. ✓ Cobalt-60 (Co-60). 5.3 years half-life. 

CELL, NERVE & MUSCLE PHYSIOLOGY

- Cell is the fundamental, structural, and functional unit of life discovered by Robert Hook in 1665.
- **Types of cells:** Prokaryotic cell (in bacteria) and Eukaryotic cell (Animal, plants, Fungi)
- **Prokaryotic cell** lacks a definite nucleus and specialized organelles, circular DNA - No Histones and divides by fission.
- **Eukaryotic cell** has a definite nucleus and organelles, Linear DNA with histones and divides by mitosis

CELL CYCLE

(Two phases: Interphase and M (mitosis) phase). The sequence is G1 – S – G2 – M



INTERPHASE	<p>Interphase is divided into G1, S, G2 phases. Barr Bodies are studied in interphase.</p> <table border="1" data-bbox="342 275 1474 594"> <tr> <td data-bbox="342 275 488 464">G1 phase</td><td data-bbox="488 275 1474 464"> <ul style="list-style-type: none"> Also called growth phase and it is the longest phase (8 - 10 hours) Highly variable and short in labile cells. G1 is between M and S phase. Primary Growth, Proteins, Organelles, mRNA Synthesis occurs in it. G1 Check point: To check if DNA is damaged. Growth factors (Insulin, EGF, PDGF, EPO) bind tyrosine kinase receptors to transition the cell from G1 to S phase. </td></tr> <tr> <td data-bbox="342 464 488 527">S phase</td><td data-bbox="488 464 1474 527"> <ul style="list-style-type: none"> Synthesis phase (5 to 6 hours). S phase is between G1 and G2. DNA Replication occurs + Cytotoxic & cancer drugs act here to destroy DNA </td></tr> <tr> <td data-bbox="342 527 488 594">G2 phase</td><td data-bbox="488 527 1474 594"> <ul style="list-style-type: none"> Secondary growth (between S phase & Mitosis), Short (3 to 4 hours) G2 phase Check point: To check if DNA has replicated properly. </td></tr> </table>	G1 phase	<ul style="list-style-type: none"> Also called growth phase and it is the longest phase (8 - 10 hours) Highly variable and short in labile cells. G1 is between M and S phase. Primary Growth, Proteins, Organelles, mRNA Synthesis occurs in it. G1 Check point: To check if DNA is damaged. Growth factors (Insulin, EGF, PDGF, EPO) bind tyrosine kinase receptors to transition the cell from G1 to S phase. 	S phase	<ul style="list-style-type: none"> Synthesis phase (5 to 6 hours). S phase is between G1 and G2. DNA Replication occurs + Cytotoxic & cancer drugs act here to destroy DNA 	G2 phase	<ul style="list-style-type: none"> Secondary growth (between S phase & Mitosis), Short (3 to 4 hours) G2 phase Check point: To check if DNA has replicated properly. 						
G1 phase	<ul style="list-style-type: none"> Also called growth phase and it is the longest phase (8 - 10 hours) Highly variable and short in labile cells. G1 is between M and S phase. Primary Growth, Proteins, Organelles, mRNA Synthesis occurs in it. G1 Check point: To check if DNA is damaged. Growth factors (Insulin, EGF, PDGF, EPO) bind tyrosine kinase receptors to transition the cell from G1 to S phase. 												
S phase	<ul style="list-style-type: none"> Synthesis phase (5 to 6 hours). S phase is between G1 and G2. DNA Replication occurs + Cytotoxic & cancer drugs act here to destroy DNA 												
G2 phase	<ul style="list-style-type: none"> Secondary growth (between S phase & Mitosis), Short (3 to 4 hours) G2 phase Check point: To check if DNA has replicated properly. 												
M PHASE	<ul style="list-style-type: none"> Mitosis (M) phase, also cytokinesis is a part of it. M is the Shortest (2 hours) <u>Features:</u> Nuclear contents divide. To see spindle assembly and alignment Genetic material is Chromosome (Genetic material is chromatid when NOT in M phase) M Divided into 06 phases : Prophase, prometaphase, Metaphase, Anaphase, Telophase, Cytokinesis <table border="1" data-bbox="342 814 1474 1188"> <tr> <td data-bbox="342 814 537 877">Prophase</td><td data-bbox="537 814 1474 877">Spindle fibers appear, Chromosome Condensation occurs. Centriole start moving to the opposite ends</td></tr> <tr> <td data-bbox="342 877 537 940">Prometaphase</td><td data-bbox="537 877 1474 940">Spindle fibers attach to chromosome & chromosome movement. Nuclear membrane dissolves marking the beginning of prometaphase</td></tr> <tr> <td data-bbox="342 940 537 1003">Metaphase</td><td data-bbox="537 940 1474 1003">Chromosome Alignment. Chromosome thickest and best studied. Chromosomes begin to divide. Karyotyping can be done in Metaphase</td></tr> <tr> <td data-bbox="342 1003 537 1066">Anaphase</td><td data-bbox="537 1003 1474 1066">Division of chromatids & sister chromatids move to opposite side. NON-Disjunction may occur here.</td></tr> <tr> <td data-bbox="342 1066 537 1157">Telophase</td><td data-bbox="537 1066 1474 1157">Spindle fibers disappear & Decondensation of Chromosomes occurs. Complete division with nuclear membrane formation chromosomal study can be done</td></tr> <tr> <td data-bbox="342 1157 537 1188">Cytokinesis</td><td data-bbox="537 1157 1474 1188">Cytoplasm divides.</td></tr> </table> <ul style="list-style-type: none"> Most affected by chemotherapy = S phase (ChemoSensitive S -- CSS) Most affected by Radiotherapy = M > G2 phase Tumors most effected by radiations = Lymphoma > Seminoma > Glioma Barr Bodies are Heterochromatin, have X chromosome (not completely inactivated) They are seen under light microscope. Absent Barr body in Turner or Scanty in Turner, helps in diagnosis of Turner syndrome One Barr body seen in Normal female > Klinefelter syndrome. Number of Barr bodies in XO = no Bar Bodies. Number of Barr bodies in XX = 1 Number of Barr bodies in XXX = 2 Barr bodies. Best for chromosomal abnormalities is Karyotyping. 	Prophase	Spindle fibers appear, Chromosome Condensation occurs. Centriole start moving to the opposite ends	Prometaphase	Spindle fibers attach to chromosome & chromosome movement. Nuclear membrane dissolves marking the beginning of prometaphase	Metaphase	Chromosome Alignment. Chromosome thickest and best studied . Chromosomes begin to divide. Karyotyping can be done in Metaphase	Anaphase	Division of chromatids & sister chromatids move to opposite side. NON-Disjunction may occur here.	Telophase	Spindle fibers disappear & Decondensation of Chromosomes occurs. Complete division with nuclear membrane formation chromosomal study can be done	Cytokinesis	Cytoplasm divides.
Prophase	Spindle fibers appear, Chromosome Condensation occurs. Centriole start moving to the opposite ends												
Prometaphase	Spindle fibers attach to chromosome & chromosome movement. Nuclear membrane dissolves marking the beginning of prometaphase												
Metaphase	Chromosome Alignment. Chromosome thickest and best studied . Chromosomes begin to divide. Karyotyping can be done in Metaphase												
Anaphase	Division of chromatids & sister chromatids move to opposite side. NON-Disjunction may occur here.												
Telophase	Spindle fibers disappear & Decondensation of Chromosomes occurs. Complete division with nuclear membrane formation chromosomal study can be done												
Cytokinesis	Cytoplasm divides.												
TYPES OF CELLS BASED ON DIVISION													
Permanent cells	<p>Remain in G0 phase and regenerate from stem cells. (G0 = resting phase). Examples: Neurons, skeletal and cardiac muscle, RBCs. RBCs never reproduce as they lack nuclei. Cells that never regenerate are: Skeletal muscle > Cardiac muscle cells > Neurons</p>												
Stable (Quiescent) cells	<p>Upon stimulation they enter G1 from G0 phase. Examples: Hepatocytes, lymphocytes, PCT and periosteal cells. Liver cells regenerate in 07 to 10 days following partial hepatectomy.</p>												
Labile cells	<p>Never go to G0, divide rapidly with a short G1, most affected by chemotherapy Examples: Bone marrow, GIT epithelium, skin, hair follicles and germ cells. GIT epithelium regenerates in 2 – 7 days.</p>												

CELL MEMBRANE & ORGANELLES	
Plasma Membrane	<ul style="list-style-type: none"> ○ Selective permeability barrier that surrounds cytoplasm of cell. According to Fluid mosaic fluid, it is a lipid bilayer in which proteins are sandwiched in mosaic manner. Composition is as follows: <ul style="list-style-type: none"> ○ Proteins 55 - 60%, Lipids 40%, Carbohydrates 5%. Thickness of cell membrane = 7.5 -10 nm ○ Lipids (40 %) <ul style="list-style-type: none"> ○ Major Lipids are Phospholipids 70%, cholesterol 13%, glycolipids 5%. Lipids act as permeability barrier and maintain fluidity (Cholesterol). Most of them are amphipathic (Polar + non-polar) ○ Head of phospholipids is Polar (Phosphate group) – Hydrophilic. ○ Tail is non-polar (long chains fatty acids) – Hydrophobic. The 2 tails form a lipid bilayer. ○ Lipid soluble substances (O₂, CO₂, steroid hormones) easily cross lipid bilayer as they can dissolve in hydrophobic lipid bilayer. ○ Water soluble substances (Na⁺, Cl⁻, glucose, H₂O) cannot dissolve in lipid bilayer, so they require water-filled channels/pores or transported by carriers. Cl⁻ is the most diffusible ion in excitable tissue. ○ Proteins (55 – 60 %) <ul style="list-style-type: none"> ○ integral proteins are imbedded in cell membrane by hydrophobic bonds or may span the membrane. They include ion channels, transport proteins, receptors, and G proteins. ○ Most of them are glycoproteins in nature. ○ Peripheral proteins are loosely attached to membrane by electrostatic interactions, they are not imbedded in cell membrane and not covalently bound to membrane components. ○ Peripheral proteins include receptors and enzymes. ○ Carbohydrates (CHO) (3- 5 %) <ul style="list-style-type: none"> ○ They are covalently bound to proteins and lipids to form glycolipids and glycoproteins ○ Glycolipids and glycoproteins are cell identity markers and help in antibody processing. ○ CHO impart -ve charge to cell, acts as receptors, help in inter-cellular attachment. ○ Glycocalyx is a loose CHO layer (Carbs moiety) on outer surface of cells. <div style="background-color: #fde9d9; padding: 5px; text-align: center;"> FACTS TO REMEMBER </div> <ul style="list-style-type: none"> ● Bonds in cell membrane → Hydrogen + Hydrophobic > Hydrophobic + covalent ● Integral proteins are joined to lipid of membrane by Hydrophobic bond ● Integral proteins joined to each other by Hydrogen > Hydrogen + Hydrophobic bond ● Peripheral proteins are attached to membrane by weak electrostatic bonds
Cytoplasm	<ul style="list-style-type: none"> ○ Cell membrane + organelles + nucleus = Protoplasm. 70-85 % of protoplasm is water. ○ Everything inside cell membrane except nucleus = cytoplasm (fluid part of protoplasm) ○ Cytosol is the soluble part of cytoplasm, and it is the site of important metabolic processes e.g glycolysis, fatty acid + proteins + purine synthesis
Nucleus	<ul style="list-style-type: none"> ○ Control centre of cell -- contains DNA and chromatin. Nucleus is double membrane bounded. ○ Most cells have a single nucleus. Mature RBCs have none. skeletal muscle cells have multiple. ○ Nuclear envelope → 2 membranes ○ Outer membrane -- in continuity with E.R. ○ Inner -- Peri nuclear membrane , with nuclear pores ○ Nuclear pores - consists of a circular arrangement of proteins surrounding a large central opening and control movement of proteins and RNA across envelope. ○ Nucleolus (dense body) → site of Ribosome Synthesis and r-RNA processing. ○ Nucleolus has no limiting membrane ○ Nucleoplasm → has enzymes (DNA Polymerase) -- Site for DNA replication + RNA synthesis
Endoplasmic Reticulum	<ul style="list-style-type: none"> ○ Rough Endoplasmic Reticulum (RER) : it has ribosomes, involved in synthesis of proteins and is continuous with nuclear membrane. ○ Smooth Endoplasmic Reticulum (SER): involved in synthesis of lipids and steroids, detoxification of alcohol (at toxic dose) and toxic substances. ○ Leydig cells and other steroids synthesizing cells have prominent SER. ○ Sarcoplasmic reticulum is a type of SER that stores and releases calcium in muscles.
Mitochondria	<ul style="list-style-type: none"> ○ It is also double membrane bounded -- 2 membranes. ○ Outer – continuous, Lipid in nature and freely permeable (allows small molecules) ○ Inner - protein in nature and has High content of Cardiolipin. It is impermeable. Inner membrane folds to form cristae.(increased surface area). Inter-membrane space has adenylate kinase. ○ Mitochondrial is the powerhouse of cell, involved in generation of free radicals and apoptosis. ○ Its Matrix-has specific Circular DNA, ribosomes, and Enzymes. It is self-replicative organelle.

	<ul style="list-style-type: none"> ○ Mitochondrial DNA is maternally inherited. Metabolic pathways operating in mitochondria are: ○ TCA cycle, Urea Cycle, Fatty acids beta Oxidation, heme synthesis (also in cytosol) 																
Ribosomes	<ul style="list-style-type: none"> ○ Sites of protein synthesis + high content of r-RNA. They are present free in cytoplasm or attached to RER. Ribosomes consists of two subunits. large subunit and small subunit ○ Prokaryotes 70S = 50 S +30 S and Eukaryotes-80 S = 60 S + 40 S 																
Golgi Complex	<ul style="list-style-type: none"> ○ Processing, packaging, modifications, labelling and delivery of proteins. ○ For example : adding carbs moiety to proteins and packaging into vesicles is done by Golgi bodies 																
Lysosomes	<ul style="list-style-type: none"> ○ Single- membrane bound, arise from Golgi apparatus, and appear as hollow structure around nucleus. Contain hydrolases, cause degradation of unfolded proteins (also called suicidal bags) ○ Uterus and breast regress after pregnancy and parturition by action of lysosomes. 																
Peroxisomes	<ul style="list-style-type: none"> ○ Single membrane bounded, arise from SER, and contains oxidase, Peroxidase, Catalases ○ Functions: Oxidation of amino acids + oxidation of long chain fatty acids. ○ Protects cell from the toxic effects of H₂O₂. Dysfunction of Peroxisomes leads to Zellweger syndrome. ○ NOTE : ○ Oxidation of Very long chain fatty acids – by Peroxisomes ○ Oxidation of short cell chain fatty acids – by Mitochondria 																
Cytoskeleton	<ul style="list-style-type: none"> ○ A network of protein filaments that extends throughout the cytoplasm and anchored to plasma membrane. Dynamic structure consisting of Three types of filamentous proteins : Microtubules, Intermediate filaments, and Microfilaments. Cytoskeleton functions include : ○ Provides shape and supporting framework to cell, helps in cell division, cell movement, muscle contraction and role in healing (microfilaments). The details of three main proteins is tabulated. <table border="1"> <tr> <td>Microtubules</td><td> <p>Largest of all, hollow structures made of tubulin subunits (alpha, beta).</p> <p>Molecular motor proteins transport cellular cargo towards opposite end of microtubules. They are dynein and kinesin.</p> <table border="1"> <tr> <td>Dynein</td><td>Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.</td></tr> <tr> <td>Kinesin</td><td>Anterograde to microtubules (-Ve → +Ve)</td></tr> </table> <p>Functions of Microtubules:</p> <ul style="list-style-type: none"> ○ They Help in movement + cell division. Examples are cilia, flagella, centrioles, mitotic spindles, and axonal trafficking. ○ Cilia = 9 doublets + 2 singlets arrangement of microtubules. ○ Basal body (base of cilium below cell membrane) = 9 triplets of microtubules with no central microtubules. ○ Axonemal dynein is an ATPase that links peripheral 9 doublets and causes bending of cilium by differential sliding of doublets. ○ Gap junctions enable coordinated ciliary movements. <p>Clinical effects: recurrent URTI + LRTI and Kartagener syndrome</p> <ul style="list-style-type: none"> ○ Kartagener syndrome: autosomal recessive Dynein arm defect leads to immotile cilia and dysfunctional Ciliated epithelium. Findings include : ○ situs inverses, Hearing loss, recurrent infections (eg, sinusitis Ear infections, bronchiectasis due to impaired Ciliary clearance of debris/pathogens), Infertility (risk of ectopic pregnancy due to dysfunctional fallopian tube cilia, immotile Spermatozoa). ○ Lab findings: ↓ nasal nitric oxide (used as screening test). </td></tr> <tr> <td>Intermediate filaments</td><td> <p>Maintain cell structure, thicker than microfilaments but thinner than microtubules. They include cytokeratin, desmin, vimentin, neurofilaments and GFAP (astrocytes marker).</p> <table border="1"> <tr> <td>Cytokeratin</td><td>Epithelial marker, resist mechanical stress, cell repair</td></tr> <tr> <td>Desmin</td><td>Muscle marker, maintain structural+ functional integrity</td></tr> <tr> <td>Vimentin</td><td>Mesenchymal marker, role in cellular attachments, migration, and signalling.</td></tr> </table> </td></tr> <tr> <td>Microfilaments</td><td> <p>Thinnest of all, Role in muscle contraction, cytokinesis, and healing(actin). Examples: actin and microvilli.</p> </td></tr> </table>	Microtubules	<p>Largest of all, hollow structures made of tubulin subunits (alpha, beta).</p> <p>Molecular motor proteins transport cellular cargo towards opposite end of microtubules. They are dynein and kinesin.</p> <table border="1"> <tr> <td>Dynein</td><td>Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.</td></tr> <tr> <td>Kinesin</td><td>Anterograde to microtubules (-Ve → +Ve)</td></tr> </table> <p>Functions of Microtubules:</p> <ul style="list-style-type: none"> ○ They Help in movement + cell division. Examples are cilia, flagella, centrioles, mitotic spindles, and axonal trafficking. ○ Cilia = 9 doublets + 2 singlets arrangement of microtubules. ○ Basal body (base of cilium below cell membrane) = 9 triplets of microtubules with no central microtubules. ○ Axonemal dynein is an ATPase that links peripheral 9 doublets and causes bending of cilium by differential sliding of doublets. ○ Gap junctions enable coordinated ciliary movements. <p>Clinical effects: recurrent URTI + LRTI and Kartagener syndrome</p> <ul style="list-style-type: none"> ○ Kartagener syndrome: autosomal recessive Dynein arm defect leads to immotile cilia and dysfunctional Ciliated epithelium. Findings include : ○ situs inverses, Hearing loss, recurrent infections (eg, sinusitis Ear infections, bronchiectasis due to impaired Ciliary clearance of debris/pathogens), Infertility (risk of ectopic pregnancy due to dysfunctional fallopian tube cilia, immotile Spermatozoa). ○ Lab findings: ↓ nasal nitric oxide (used as screening test). 	Dynein	Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.	Kinesin	Anterograde to microtubules (-Ve → +Ve)	Intermediate filaments	<p>Maintain cell structure, thicker than microfilaments but thinner than microtubules. They include cytokeratin, desmin, vimentin, neurofilaments and GFAP (astrocytes marker).</p> <table border="1"> <tr> <td>Cytokeratin</td><td>Epithelial marker, resist mechanical stress, cell repair</td></tr> <tr> <td>Desmin</td><td>Muscle marker, maintain structural+ functional integrity</td></tr> <tr> <td>Vimentin</td><td>Mesenchymal marker, role in cellular attachments, migration, and signalling.</td></tr> </table>	Cytokeratin	Epithelial marker , resist mechanical stress, cell repair	Desmin	Muscle marker , maintain structural+ functional integrity	Vimentin	Mesenchymal marker , role in cellular attachments, migration, and signalling.	Microfilaments	<p>Thinnest of all, Role in muscle contraction, cytokinesis, and healing(actin). Examples: actin and microvilli.</p>
Microtubules	<p>Largest of all, hollow structures made of tubulin subunits (alpha, beta).</p> <p>Molecular motor proteins transport cellular cargo towards opposite end of microtubules. They are dynein and kinesin.</p> <table border="1"> <tr> <td>Dynein</td><td>Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.</td></tr> <tr> <td>Kinesin</td><td>Anterograde to microtubules (-Ve → +Ve)</td></tr> </table> <p>Functions of Microtubules:</p> <ul style="list-style-type: none"> ○ They Help in movement + cell division. Examples are cilia, flagella, centrioles, mitotic spindles, and axonal trafficking. ○ Cilia = 9 doublets + 2 singlets arrangement of microtubules. ○ Basal body (base of cilium below cell membrane) = 9 triplets of microtubules with no central microtubules. ○ Axonemal dynein is an ATPase that links peripheral 9 doublets and causes bending of cilium by differential sliding of doublets. ○ Gap junctions enable coordinated ciliary movements. <p>Clinical effects: recurrent URTI + LRTI and Kartagener syndrome</p> <ul style="list-style-type: none"> ○ Kartagener syndrome: autosomal recessive Dynein arm defect leads to immotile cilia and dysfunctional Ciliated epithelium. Findings include : ○ situs inverses, Hearing loss, recurrent infections (eg, sinusitis Ear infections, bronchiectasis due to impaired Ciliary clearance of debris/pathogens), Infertility (risk of ectopic pregnancy due to dysfunctional fallopian tube cilia, immotile Spermatozoa). ○ Lab findings: ↓ nasal nitric oxide (used as screening test). 	Dynein	Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.	Kinesin	Anterograde to microtubules (-Ve → +Ve)												
Dynein	Retrograde to microtubules (+Ve → -Ve). Rabies virus, polio virus, clostridium tetani toxin and HSV 1,2 use dynein.																
Kinesin	Anterograde to microtubules (-Ve → +Ve)																
Intermediate filaments	<p>Maintain cell structure, thicker than microfilaments but thinner than microtubules. They include cytokeratin, desmin, vimentin, neurofilaments and GFAP (astrocytes marker).</p> <table border="1"> <tr> <td>Cytokeratin</td><td>Epithelial marker, resist mechanical stress, cell repair</td></tr> <tr> <td>Desmin</td><td>Muscle marker, maintain structural+ functional integrity</td></tr> <tr> <td>Vimentin</td><td>Mesenchymal marker, role in cellular attachments, migration, and signalling.</td></tr> </table>	Cytokeratin	Epithelial marker , resist mechanical stress, cell repair	Desmin	Muscle marker , maintain structural+ functional integrity	Vimentin	Mesenchymal marker , role in cellular attachments, migration, and signalling.										
Cytokeratin	Epithelial marker , resist mechanical stress, cell repair																
Desmin	Muscle marker , maintain structural+ functional integrity																
Vimentin	Mesenchymal marker , role in cellular attachments, migration, and signalling.																
Microfilaments	<p>Thinnest of all, Role in muscle contraction, cytokinesis, and healing(actin). Examples: actin and microvilli.</p>																

CELL ARCHITECTURE

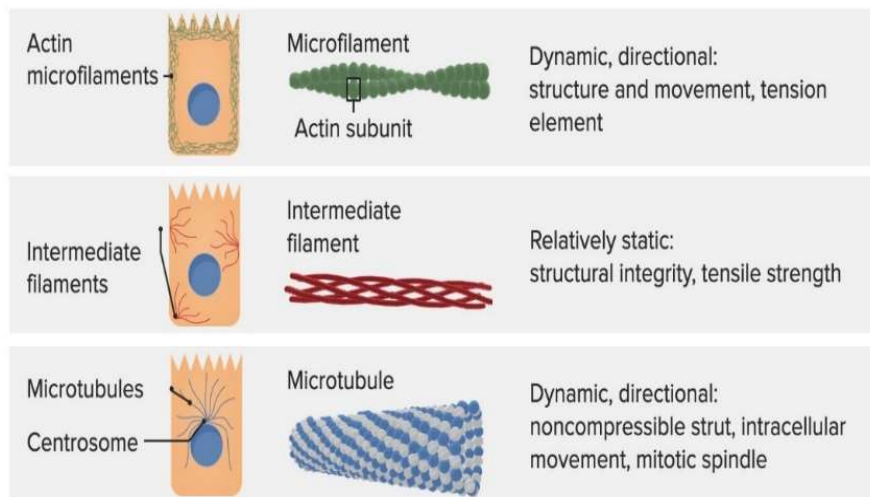
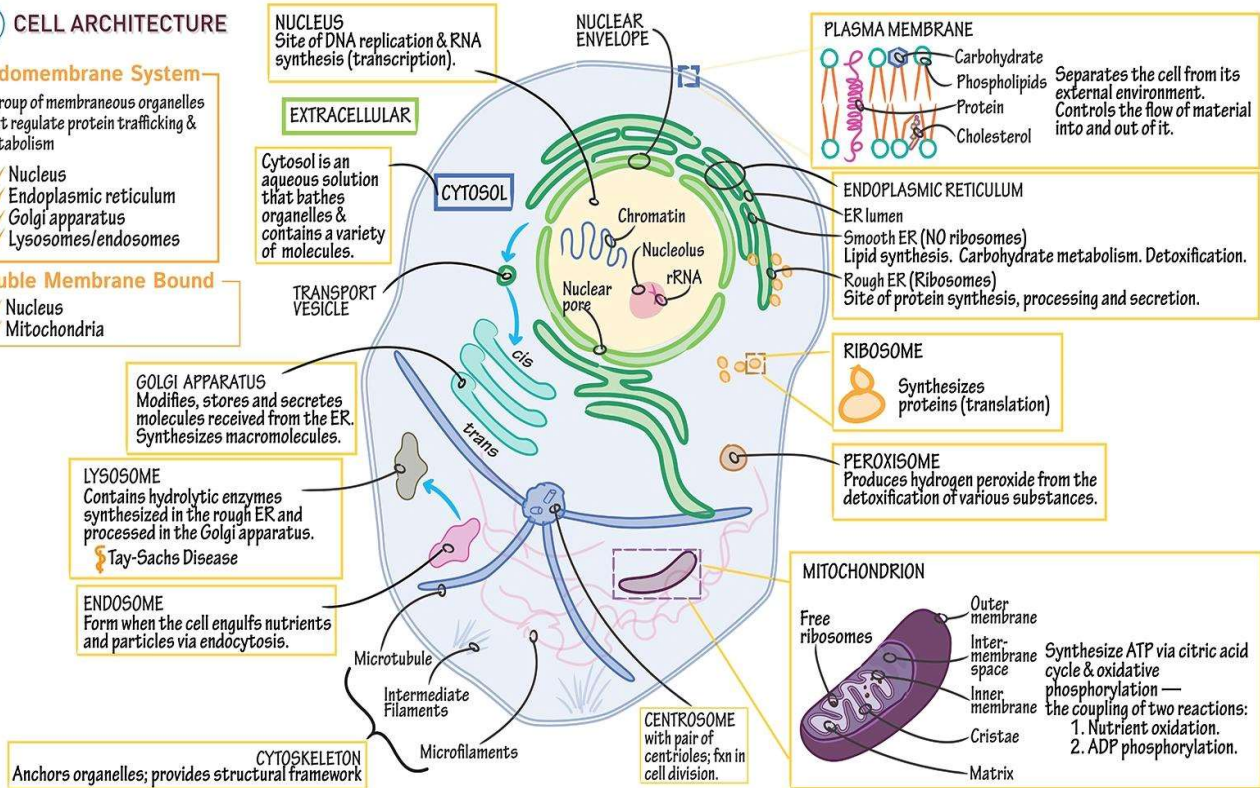
Endomembrane System

A group of membranous organelles that regulate protein trafficking & metabolism

- ✓ Nucleus
- ✓ Endoplasmic reticulum
- ✓ Golgi apparatus
- ✓ Lysosomes/endosomes

Double Membrane Bound

- ✓ Nucleus
- ✓ Mitochondria



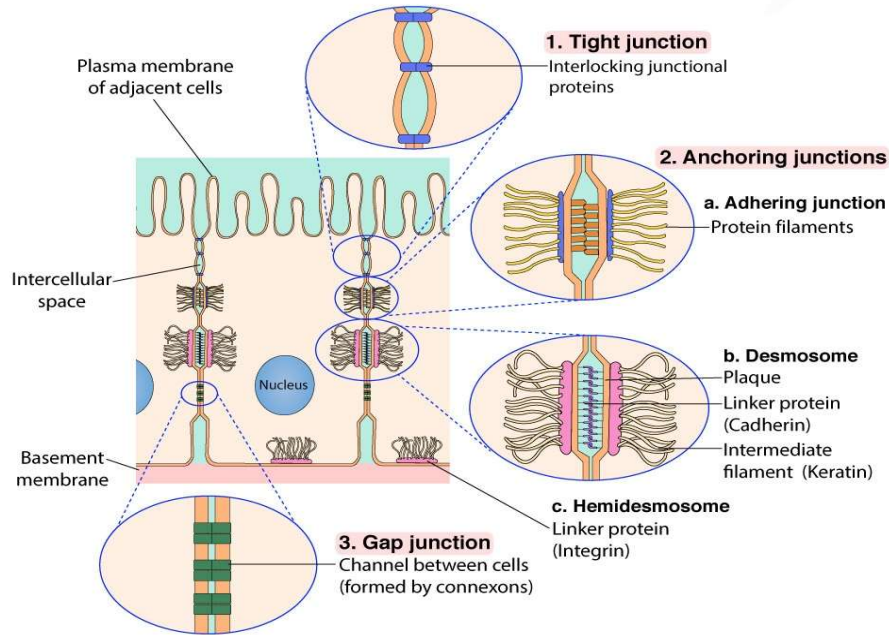
CELLULAR JUNCTIONS

- Cell junctions are the structures where long-term association between neighbouring cells are established.
- The 3 common kinds of Apical region junctions are tight Junctions, adhesive/anchoring Junctions, and gap or communicating junctions.
- The intracellular attachment proteins form a thick layer of Fibrous material on the cytoplasmic side of the plasma Membrane called a **plaque** which binds actin microfilaments in Adherent junctions and intermediate filaments in desmosomes and hemidesmosomes.
- The transmembrane linker protein is anchored to the plaque by cytoplasmic domain and binds the ECM or to the same Proteins on other cells.

Tight Junctions	<ul style="list-style-type: none"> ▪ Also known as zona occludens – made of claudins or occludens, prevent paracellular movements of solutes between cells. ▪ Epithelial cells are connected by tight junctions. ▪ They may be tight i.e impermeable (e.g in DCT of kidneys) or may be leaky/permeable as in PCT and gallbladder. ▪ Tight junctions help to keep a cell Polarized. ▪ They leave No space between Plasma membranes of adjacent cells to prevent the movement of molecules across cell layers e.g blocking the basolateral movement of glucose/ Amino acids across cells.
Adhering junctions	<ul style="list-style-type: none"> ▪ Below the tight junctions are the zonula adherens/belt desmosomes that connect actin filaments of adjacent cells by Cadherins (Ca^{+2} dependent adhesion proteins). ▪ Downregulation or loss of E – cadherins causes → Metastasis. ▪ Zonula adherens or focal adhesions connect a cell to Extracellular matrix through fibronectin receptors.
Gap Junctions	<ul style="list-style-type: none"> ▪ They are made of connexins, responsible for Attachments between cells that permit electric and chemical communication. ▪ Gap junctions allow communication in myocardial cells by current flow.
Macula adherens or Desmosomes	<ul style="list-style-type: none"> ○ Macula adherens /Spot Desmosomes connect the intermediate filaments to provide structural support. ○ Desmosomes consist of desmogleins and desmocollins. ○ Autoantibodies to desmosomes → Pemphigus vulgaris disease
Hemidesmosomes	<ul style="list-style-type: none"> ○ They connect a cell to its basement membrane by integrins or they connect keratin to the cells in basal layer. ○ Autoantibodies against hemidesmosomes → Bullous pemphigus disease.
Integrins	<ul style="list-style-type: none"> ○ Membrane proteins that maintain integrity of basolateral membrane by binding to collagen and laminin to basement membrane. ○ Integrins link a cell to its extracellular matrix (ECM)
KEY FACTS	

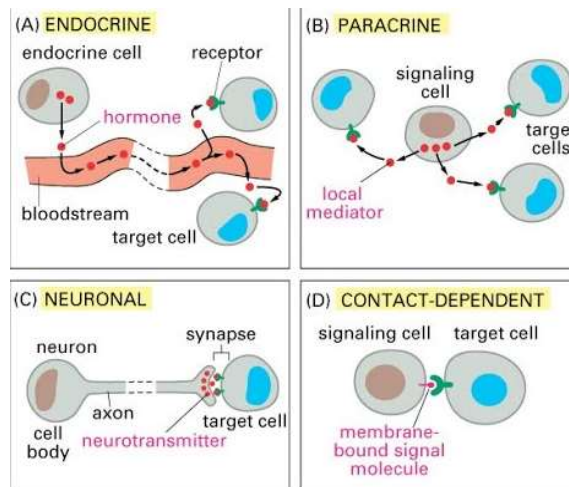
- Connexins make Gap Junctions – they allow electrical and chemical communication e.g in Heart.
- Occludens, Claudin, Zonulin & Catenin are related to Tight Junctions.
- **Epithelial cells are connected by tight junctions.**
- Cell to Basement membrane adhesion is mediated by Hemidesmosomes.
- Cell to cell adhesion is mediated by Desmosomes (through Cadherins).
- **Cytoskeleton to ECM connection via Integrins**
- ECM & cytoskeleton communicate across the cell membrane by Integrins
- Cell-Cell Desmosome → Cadherins (connect actin filaments of adjacent cells).
- **Responsible for Cell-to-Cell adhesion during embryonic development → Cadherin's**
- Cell-Cell binding (Desmosome) → consists of Desmocollins & Desmogleins
- Zonula adherens/Belt Desmosomes related to → E-Cadherins
- **ECM is connected to ICM via Intermediate filaments.**

Types of Cell Junctions



CHEMICAL SIGNALLING

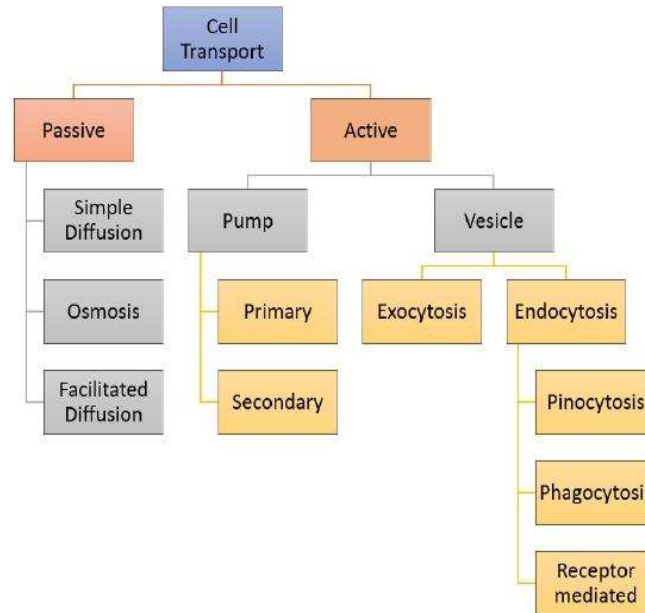
- Autocrine signalling:** A cell targets itself
- Paracrine signalling:** A cell signals nearby cell, both autocrine + paracrine occurs via diffusion in interstitial fluid
- Paracrine signalling is seen in Thymus.** Paracrine uses local mediators e.g prostaglandins and hormones e.g estrogen.
- Endocrine signalling:** A cell targets a distant cell Through the bloodstream
- Direct signalling :** A cell targets a neighbouring cell through a gap junction
- Synaptic transmission:** junction between a nerve fiber and a muscle fiber or between 2 nerve fibers using neurotransmitter for signal transmission.



TRANSPORT ACROSS CELL / CELL MEMBRANE

Two main types: passive and active type

- ❖ **Passive** requires no energy e.g simple diffusion or facilitated diffusion.
- ❖ **active** requires energy in the form of ATP e.g primary active or secondary active
- ❖ **Carrier mediated transport** uses a carrier, it includes facilitated diffusion + primary & secondary active transport.

**Simple Diffusion**

- Movement of substances across cell membrane down an electrochemical gradient (downhill) i.e from higher concentration to lower concentration, using no energy and without any carrier protein.
- **Permeability** is the ease by which a solute diffuses through a membrane. It depends on features of solute and membrane. **Factors that affect permeability also affect the diffusion.**
- Factors that **↑** permeability are:
 - ✚ **↑** lipid solubility or oil/water coefficient, **↓** size of solute will increase permeability and speed of diffusion,
 - ✚ **↓** thickness of membrane will increase permeability and diffusion vice versa.

FACTORS AFFECTING DIFFUSION

↑ Concentration gradient → **↑** diffusion
↑ Temperature will increase diffusion rate
↑ Oil/water partition co-efficient or higher the lipid solubility, will increase diffusion rate
↑ **Surface area** of membrane will **↑** diffusion

↓ Size of particles will increase diffusion
↑ **membrane thickness** will decrease diffusion
↑ gradient size or diffusion distance will increase the rate of diffusion

Facilitated Diffusion

- Movement of substances across cell membrane down an electrochemical gradient (downhill) using a carrier protein without utilization of energy.
- Example: The transport of glucose in muscle and adipose tissue, placenta is via facilitated diffusion
- Factors that affect simple diffusion also effect the facilitated transport.

Characteristics Of Carrier-Mediated Transport**Saturation**

- Transport rate increases as the solute concentration increases until the carriers are saturated e.g transport maximum of glucose (T_m) is analogous to the maximum velocity in enzyme kinetics.

Competition

- Structurally related solutes compete for transport sites on carriers e.g galactose is a competitive inhibitor of glucose transport in the small intestine

	<p>Stereospecificity</p> <ul style="list-style-type: none"> ○ D glucose (natural isomer) is transported by facilitated diffusion but L- glucose isomer is not. In contrast, simple diffusion will not differentiate between these two as it does not involve any carrier.
Primary Active Transport	<ul style="list-style-type: none"> ○ Occurs against an electrochemical gradient (Uphill) i.e from an area of lower to higher concentration using a carrier and energy in the form of ATP (therefore called active transport). ○ As it involves a carrier, so it exhibits Stereospecificity, Saturation and competition. <p>Examples:</p> <ul style="list-style-type: none"> • Na⁺, K⁺ -ATPase (Na⁺ -- K⁺ pump): located in the plasma Membrane with ATP site on cytosolic side, for each ATP consumed, 2 K⁺ go into the cell (pump dephosphorylated) and 3 Na⁺ go out of the cell (pump phosphorylated). Digitalis and Ouabain block this pump which indirectly inhibits the Na/Ca exchanger → increased intracellular Ca⁺, leads to increased contractility of heart. • Ca²⁺ ATPase (Ca²⁺pump): present in cell membrane and sarcoplasmic reticulum, transports Ca²⁺ against the gradient. • H⁺, K⁺ ATPase (Proton pump): present in gastric parietal cells and alpha intercalated cells of renal collecting tubules transports H⁺ into lumen (of stomach/renal tubules) against the gradient. Omeprazole blocks this proton pump irreversibly that helps in acid peptic disease and peptic ulcers.
Secondary Active Transport	<p>Energy is not directly provided by ATP, but it is provided by concentration gradient of Sodium (Na⁺)</p> <p>One solute moves (usually Na⁺) downhill providing energy for the other solute, either in same direction (co-transport) or opposite direction (counter-transport) e.g Na⁺-glucose co-transport. 2nd ry active transport may be symport (co-transport) if movement occurs in same direction or anti-port (counter transport) if movement occurs in opposite direction.</p> <p>Na⁺, Glucose Co-transport or Symport: If the solutes move in the same direction across the cell membrane, it is called Cotransport or symport. Glucose is transported "uphill"; Na⁺ is transported "downhill". Energy is derived from the "downhill" movement of Na⁺</p> <p>Na⁺, Ca²⁺ counter transport or Antiport: Ca moves uphill while Na moves in opposite direction (downhill) providing energy. in this process substance is transported in exchange of sodium ions</p>

BULK TRANSPORT

It involves transport by formation of membrane bound vesicles e.g transport of macromolecule that Requires ATP, Ca²⁺

Exocytosis

Expulsing molecules out from the cell.

Fate of molecule released by exocytosis may be:

Peripheral proteins, Part of extracellular matrix or released to extracellular medium

Endocytosis

Engulfing large molecules by the cell Two type of endocytosis :

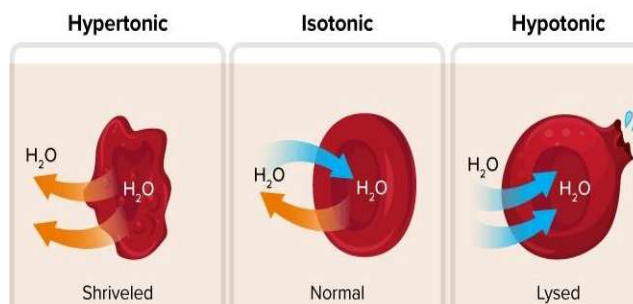
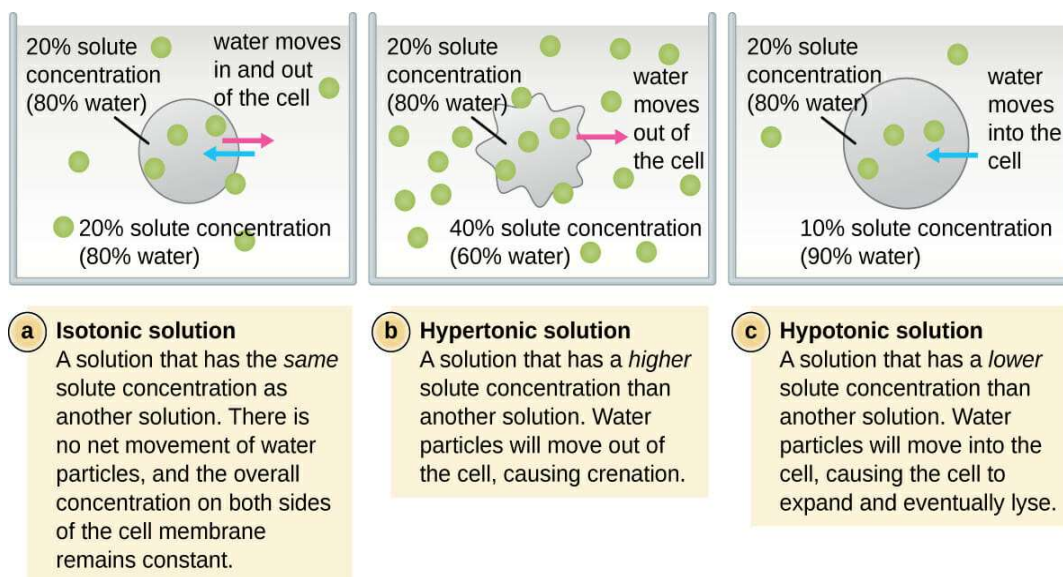
Phagocytosis/cell eating involves ingestion of large molecules, such as bacteria into the cell. It occurs only in specialized cells e.g WBC engulf bacteria.

Pinocytosis/cell drinking is the Uptake of fluid/fluid contents into the cell and occurs in all cells. Substances having molecular weight > 1000 cross by pinocytosis. Actin, myosin, Clathrin involved.



Receptor mediated endocytosis uses membrane protein **Clathrin** coated vesicles.

OSMOSIS






















- ❖ It is defined as the movement of water (or any other solvent) from low solute concentration to higher solute concentration through a semipermeable membrane.
- ❖ In osmosis, only the solvent moves in contrast to diffusion in which both solute and solvent move.
- ❖ Colloid osmotic or Oncotic pressure is the osmotic pressure created by proteins e.g., plasma proteins
- ❖ Osmolality is the No. of osmoles of solute per litre of water is called osmolality
- ❖ Osmole is the unit used to express the concentration of a solution in terms of numbers of particles in place of grams
 - One osmole is 1-gram molecular weight of osmotically active solute. Thus, 180 grams of glucose, which is 1-gram molecular weight of glucose, is Equal to 1 osmole of glucose because glucose does not dissociate into ions. Conversely, if a solute dissociates into two ions, e.g., NaCl 1-gram molecular Weight of the solute will become 2 osmoles.
- Osmolarity is the Concentration of osmotically active particles in a solution
 - Osmolarity = $g \times C$ (Where g =number of particles in a solution and C - concentration)
 - E.g., what is the Osmolarity of a 1M NaCl solution
 - Osmolarity = $g \times C = 2 \text{ Osm/mol} \times 1\text{M} \rightarrow 2 \text{ Osm/L}$ answer
- ❖ Two solutions having the same osmolarity are called **isosmotic** e.g. 0.9% NaCl and RL relative to blood
- ❖ The solution having higher osmolarity is called **Hyperosmotic** e.g 3% NaCl
- ❖ The solution having lower osmolarity is called **hyposmotic** e.g 0.5% DW and 0.45% NaCl
- ❖ Pressure required to stop osmosis completely is called **osmotic pressure** and calculated by van't Hoff's law
- ❖ It Depends on the concentration of osmotically active particles, Increases when the solute concentration increases





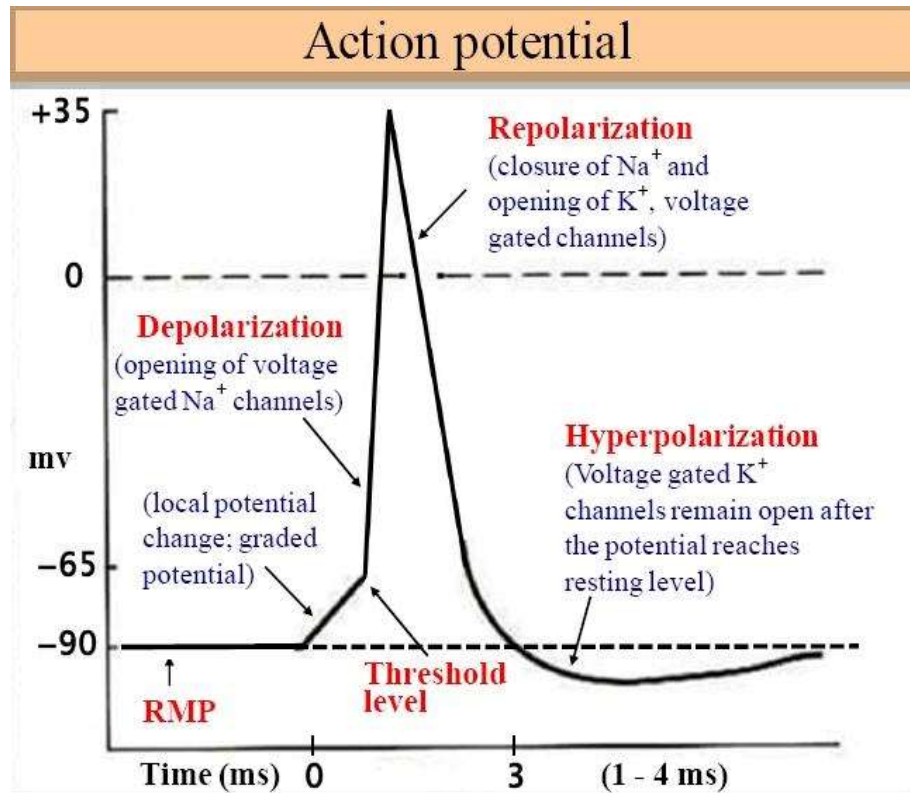
KEY FACTS – ORGANELLES & CELLULAR TRANSPORT

- Diameter or thickness of cell membrane is 7.5 – 10 nm. 55-60% protein and 40% lipids present in cell membrane.
- Protoplasm has 70-85% water. Nissle Substance is related to RER in neurons
- Nucleolus has no limiting membrane. Centrioles make Basal body (basal body makes cilia and flagella)
- RER is Continuous with Nuclear membrane. Ribosomes and cytoskeleton have no limiting membrane
- Detoxification of drugs and detoxification of Alcohol at Toxic dose occurs in SER
- Detoxification of Alcohol at Normal Dose occurs in peroxisomes
- Lysosomes Contain Hydrolytic enzyme and peroxisomes has Oxidase H₂O₂)
- Peroxisome Originate from SER but Lysosome Originate from Golgi Bodies
- VLFA Oxidation occurs in Peroxisome and short chain FA oxidation at Mitochondria
- Generation of free radicals is done by mitochondria. Mitochondria has own DNA, and it is self-replicative.
- Leydig Cell and steroid synthesizing cells have abundant SER
- Mitochondria : Powerhouse + self-replicating + Short chains Fatty acids Metabolism
- Double membrane bounded organelles Nucleus and Mitochondria
- Golgi bodies involved in Packaging, processing, and modification.
- Production of proteins is the role of Ribosomes > RER
-  Size of particles will increase diffusion and  membrane thickness will decrease diffusion
- Glucose is transported to placenta by Facilitated Diffusion
- Glucose transport across membrane due to its concentration difference by Facilitated Diffusion
- Glucose is absorbed in renal tubules through secondary active Transport
- Amino acids are absorbed from kidney to blood by secondary active Transport
- Substances/drugs having molecular weight < 1000, their Transport occurs via Diffusion
- Substances/drugs having molecular weight is > 1000 Transport occurs via Pinocytosis
- Chloride and Urea are transported by Passive Diffusion/Simple diffusion
- Oxygen uptake in lungs occurs through Simple Diffusion (Passive)
- Local Anaesthesia crosses Placenta by Simple Diffusion (Passive)
- The membrane protein Clathrin is involved in – Receptor mediated Endocytosis
- Transport through cell membrane involving Actin, Myosin and Clathrin is called pinocytosis
- In secondary active transport energy is NOT directly provided by ATP, but through conc. Gradient of Na⁺

Ion Channels, Diffusion Potential, Resting Membrane Potential & Action Potential

Ion Channels	<ul style="list-style-type: none"> ○ They are integral proteins that span the membrane and invaginated to form pores, their opening and closing are controlled by gates using 2 principal ways (Voltage/Ligand gated) ○ Ion channels are selective; they permit the passage of some ions, but not others. ○ Selectivity is based on the size of the channel and the distribution of charges that line it. ○ Ion channels may be open or closed. When the channel is open, the ion(s) for which it is selective can flow through. When the channel is closed, the ions cannot flow through. ○ The conductance of a channel depends on the probability that the channel is open. <table border="1" data-bbox="446 1417 1443 1902"> <tr> <td data-bbox="446 1417 633 1774">Voltage gated channels</td><td data-bbox="633 1417 1443 1774"> <ul style="list-style-type: none">  They are opened or closed by changes in membrane potential.  The activation gate of the Na channel in nerve is opened by depolarization.  The inactivation gate of the Na channel in nerve is closed by depolarization.  When both the activation and inactivation gates on Na channels are open, the channels are open and permeable to Na (during the upstroke of the nerve action potential)  If either the activation or inactivation gate on the Na channel is closed, the channel is closed and impermeable to Na. For example, at the resting potential, the activation Gates are closed -- the Na channels are closed </td></tr> <tr> <td data-bbox="446 1774 633 1902">Ligand-gated channels</td><td data-bbox="633 1774 1443 1902"> <ul style="list-style-type: none">  They are opened or closed by hormones, 2nd messengers, or Neurotransmitters,  For example, the nicotinic receptor for acetylcholine (Ach) at the motor end plate is an Ion channel that opens when Ach binds to it. When </td></tr> </table>	Voltage gated channels	<ul style="list-style-type: none">  They are opened or closed by changes in membrane potential.  The activation gate of the Na channel in nerve is opened by depolarization.  The inactivation gate of the Na channel in nerve is closed by depolarization.  When both the activation and inactivation gates on Na channels are open, the channels are open and permeable to Na (during the upstroke of the nerve action potential)  If either the activation or inactivation gate on the Na channel is closed, the channel is closed and impermeable to Na. For example, at the resting potential, the activation Gates are closed -- the Na channels are closed 	Ligand-gated channels	<ul style="list-style-type: none">  They are opened or closed by hormones, 2nd messengers, or Neurotransmitters,  For example, the nicotinic receptor for acetylcholine (Ach) at the motor end plate is an Ion channel that opens when Ach binds to it. When
Voltage gated channels	<ul style="list-style-type: none">  They are opened or closed by changes in membrane potential.  The activation gate of the Na channel in nerve is opened by depolarization.  The inactivation gate of the Na channel in nerve is closed by depolarization.  When both the activation and inactivation gates on Na channels are open, the channels are open and permeable to Na (during the upstroke of the nerve action potential)  If either the activation or inactivation gate on the Na channel is closed, the channel is closed and impermeable to Na. For example, at the resting potential, the activation Gates are closed -- the Na channels are closed 				
Ligand-gated channels	<ul style="list-style-type: none">  They are opened or closed by hormones, 2nd messengers, or Neurotransmitters,  For example, the nicotinic receptor for acetylcholine (Ach) at the motor end plate is an Ion channel that opens when Ach binds to it. When 				

		open, it is permeable to Na and K, causing the motor end plate to depolarize						
Diffusion potential	<ul style="list-style-type: none">The potential difference generated across a membrane due to concentration difference of an ion and can be generated only if the membrane is permeable to the ion.The size of the diffusion potential depends on the size of the concentration gradient.							
Equilibrium potential	<ul style="list-style-type: none">The equilibrium potential is the potential difference that would exactly balance (oppose) the tendency for diffusion down a concentration difference.At electrochemical equilibrium, the chemical and electrical driving forces that act on an ion are equal and opposite and no further net diffusion of the ion occurs.It is calculated from Nernst equation. Values for Equilibrium potential for ions are as follows;E_{Na^+} (+65mV), E_{K^+} (-85 mV), E_{Cl^-} (-85 mV), $E_{Ca^{++}}$(+120 mV)							
Membrane potential	<ul style="list-style-type: none">Electric potential across membrane is the membrane potential.At rest outside is +Ve and inside the membrane is -Ve (due to proteins, PO4)At actions potential outside becomes -Ve and inside +Ve (less -Ve)							
Driving force and current flow	<ul style="list-style-type: none">The driving force on an ion is the difference between the actual membrane potential (E_m) and the ion's equilibrium potential (calculated with the Nernst equation)Current flow occurs if there is a driving force on the ion and the membrane is permeable to the ion. The direction of current flow is in the same direction as the driving force. The magnitude of current flow is determined by the size of the driving force and permeability/conductance) of ion.							
Resting membrane potential (RMP)	<ul style="list-style-type: none">is the Membrane potential of nerve fiber at rest or when it is not transmitting signals.RMP = -70 mV inside, contributed by Na/K electrogenic pump that transports 3 Na⁺ ions inside and 2 K⁺ ions towards outside, thus creating negativity inside.At rest, membrane is more leaky to K⁺ as compared to Na⁺ ions, hence, RMP is the result of high resting conductance to K⁺ ions. RMP is achieved by K⁺ efflux and maintained via Na⁺,K⁺ ATPase.At rest, the inactivation gates on Na⁺ channel are open, the activation gates are closed and thus the Na⁺ channel are closed and Na⁺ conductance is low.							
Action potential (AP)	<ul style="list-style-type: none">A stimulus leads to change in membrane potential from normal -Ve value at rest (RMP = -70 mV) to +Ve value and then back to -Ve giving rise to impulse, that is called AP.Threshold potential is the membrane potential at which AP occurs. At threshold, net inward current becomes larger than net outward current, thus giving rise to AP.If net inward current is less than outward current, → No AP will occur.Action potential follows All or none response: As long as the stimulus meets threshold, AP will occur. Magnitude of AP is independent of stimulus strength → once threshold is reached, the amplitude of all APs will be constant i.e the size of AP is always the same.You can't have a short AP, either it will occur, or it will not occur at all <p>Conduction velocity increases by  diameter size,  myelination.</p> <p>Stages of AP are as follows:</p> <table><tr><td>Depolarization</td><td>Due to Na⁺ influx via voltage gated Na channels, depolarization makes the membrane potential less negative (more +Ve)</td></tr><tr><td>Repolarization</td><td>Due to K⁺ efflux via voltage gated K⁺ channels, it makes the membrane potential more -Ve</td></tr><tr><td>Hyperpolarization</td><td>After AP is over, K⁺ channels remain opened and membrane potential becomes closer to the K⁺ equilibrium potential.</td></tr></table>		Depolarization	Due to Na⁺ influx via voltage gated Na channels, depolarization makes the membrane potential less negative (more +Ve)	Repolarization	Due to K⁺ efflux via voltage gated K ⁺ channels, it makes the membrane potential more -Ve	Hyperpolarization	After AP is over, K⁺ channels remain opened and membrane potential becomes closer to the K ⁺ equilibrium potential.
Depolarization	Due to Na⁺ influx via voltage gated Na channels, depolarization makes the membrane potential less negative (more +Ve)							
Repolarization	Due to K⁺ efflux via voltage gated K ⁺ channels, it makes the membrane potential more -Ve							
Hyperpolarization	After AP is over, K⁺ channels remain opened and membrane potential becomes closer to the K ⁺ equilibrium potential.							



REFRACTORY PERIOD

Period during which a 2nd action potential can't occur in presence of first action potential is called Refractory period.

- **Absolute Refractory Period:** Period during which a **2nd AP cannot be elicited** even with a very strong stimulus
Cause: shortly after Na^+ channels are opened to cause depolarization they become inactivated and cannot be reopened to cause another depolarization by any number of stimuli. E.g., during depolarization
- **Relative Refractory Period:** Period during which stronger than normal stimuli can cause a second action potential.
Cause: most of Na^+ channels have been reversed from their state of inactivation e.g., during Repolarization.

KEY FACTS

- RMP (-70 mV) is achieved by K^+ efflux and maintained by Na^+ , K^+ – ATPase pump

Height of AP is Related to Sodium

Hypernatremia → increase height of action potential
 Hyponatremia → decrease height of action potential

Excitability Related to Potassium

Hyperkalemia → Increase Excitability of neuron at AP
 Hypokalemia → Decrease Excitability of neuron at AP

Relation of Calcium

High Ca^{2+} inhibits Na^+ movement by voltage gated Na^+ channels
 Hypercalcemia → decreased Neuronal excitability
 Hypocalcemia → Increased Excitability of neuron

NEUROMUSCULAR AND SYNAPTIC TRANSMISSION

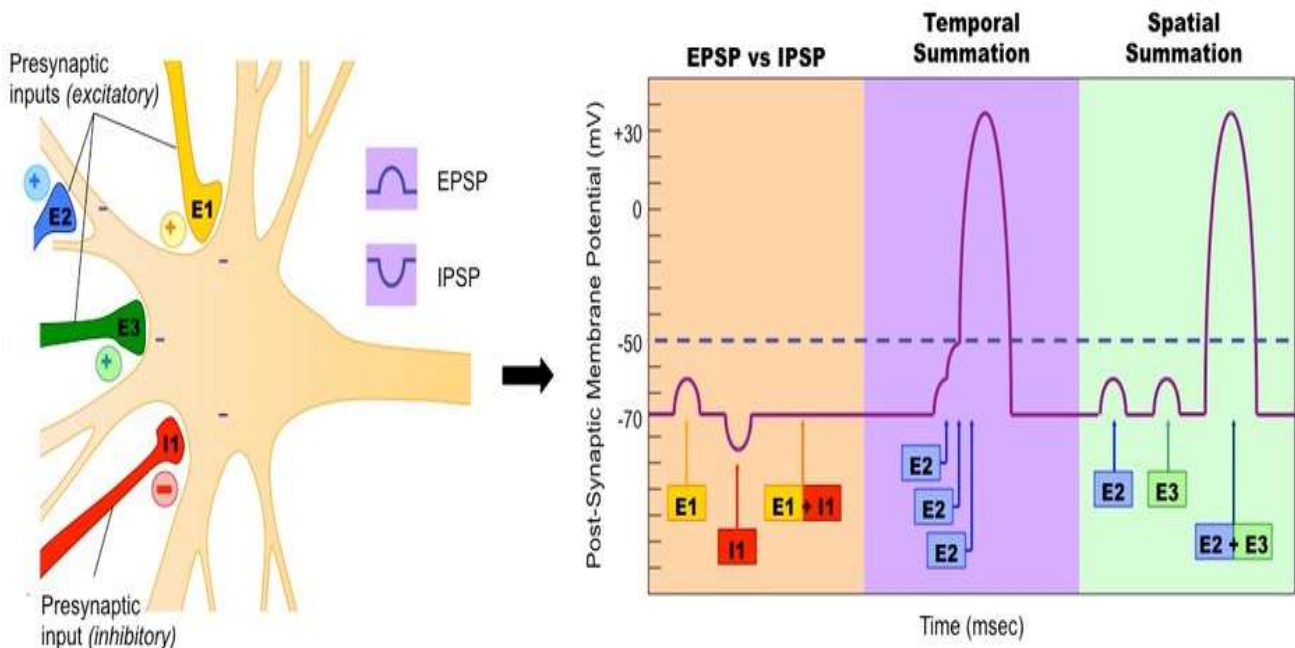
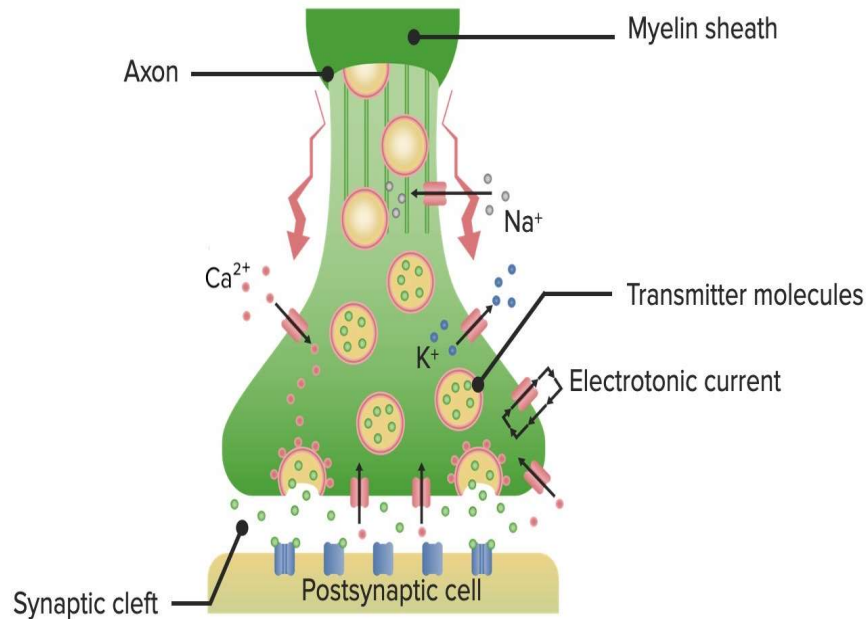
- Junction between excitable cells that allows transmission of a signal is called Synapses e.g neuromuscular junction
- **Neuromuscular junction (NMJ):** Synapse between nerve ending (axons) and muscle membrane is NMJ
- The neurotransmitter released from the presynaptic terminal is Ach, and the postsynaptic membrane has a nicotinic receptor. Axon terminal contains mitochondria and synaptic vesicles.
- **Synaptic vesicles contain the Neurotransmitter substance, acetylcholine (Ach).**
- An action potential in the presynaptic cell causes depolarization of the Presynaptic terminal, **Ca enters into presynaptic terminal causing release of neurotransmitter into synaptic cleft.**
- Neurotransmitter combines with receptors on post synaptic Cell membrane causing a change in its permeability to ions and consequently change in action potential.
- Inhibitory neurotransmitters hyperpolarize and excitatory ones depolarize the postsynaptic membrane.
- **End plate potential (EPP):** When Ach gated channels open due to arrival of Nerve action potential, sudden influx of Na⁺ influx into muscle fiber causes membrane potential to rise in +Ve direction this is called end plate potential.
- EPP is not an action potential but initiate and propagate action
- **Miniature end plate potential:** Under resting condition, occasional ACh vesicles fuse with membrane and release small amounts of Ach that causes a small potential called miniature end plate potential (MEPP).
- MEPP summate to produce full-fledged Excitatory post-synaptic potential (EPP).
- Ach is degraded by Ach-esterase (AChE) enzyme to acetyl CO-A and choline, half of choline is taken back into presynaptic ending by Na⁺ Choline cotransport and used to Synthesize the new Ach.
- **Botox (botulinum toxin)** blocks release of Ach from presynaptic terminal → Total blockade of NM transmission
- **Neostigmine** is Acetylcholinesterase inhibitor. Thus prolong EPP by **↑** Ach at muscle end plate
- **Curare** (e.g Tubocurarine) compete with Ach on motor end plate → decrease the size of EPP
- **Hemicholinium** blocks reuptake of choline into presynaptic terminal → depletes the Ach stores at presynaptic end.

INPUT TO SYNAPSES

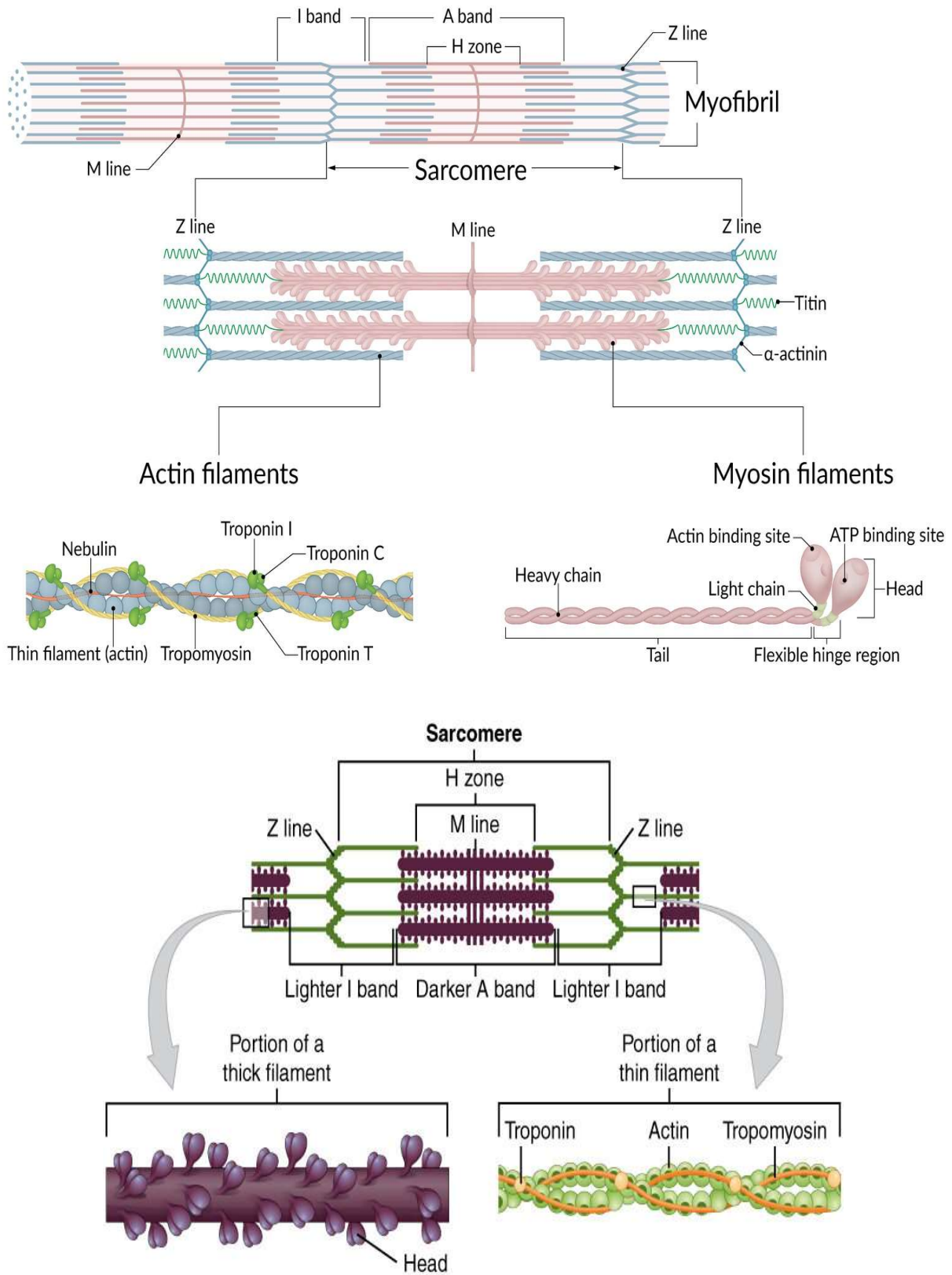
- The postsynaptic cell integrates excitatory and inhibitory inputs.
 - When the sum of the input brings the membrane potential of the postsynaptic cell to threshold, it fires AP
 - Acidosis, hypoxia, and anaesthesia **↓** synaptic transmission. Alkalosis, caffeine, theophylline **↑** transmission
1. **Excitatory Postsynaptic Potentials (EPSPs)** are inputs that depolarize the postsynaptic cell, bringing it closer to threshold and closer to action potential, caused by opening of channels that are permeable to Na⁺ and K⁺, like the Ach Channels.
Excitatory neurotransmitters include Ach, norepinephrine, epinephrine, dopamine, **glutamate**, and serotonin
 2. **Inhibitory Postsynaptic Potentials (IPSPs)** are the inputs that hyperpolarize the postsynaptic cell, moving it away from threshold and farther from firing an action potential, caused by opening Cl channels.
Inhibitory neurotransmitters are **γ-aminobutyric acid (GABA) and glycine**.

SUMMATION AT SYNAPSES

- **Spatial summation:** occurs when excitatory potentials from many different presynaptic neurons cause the postsynaptic neuron to reach its threshold and fire
- **Temporal summation:** occurs when a single presynaptic neuron fires many times in succession causing the postsynaptic neuron to reach its threshold and fire.



SKELETAL MUSCLE					
	<p>They are of voluntary nature and striated in appearance.</p> <p>Each muscle fiber is multinucleate and behaves as a single unit.</p> <p>It contains bundles of myofibrils surrounded by SR and invaginated by T tubules</p>				
Muscle Fiber	<p>It is the structural and functional unit of muscle. Composition of muscle fiber as follows:</p> <ul style="list-style-type: none"> • Sarcolemma is the cell membrane of muscle fiber that surrounds it • Sarcoplasm is the matrix of muscle fiber • Sarcoplasmic reticulum contains protein Calsequestrin which binds Ca^{+2} (40 times more) • Myofibrils made of 1500 thick (myosin) and 3000 thin (actin) filaments. • Each muscle fiber is innervated by one nerve ending at center 				
Myofibrils	<p>They are made of thick (myosin) and thin (actin) filaments. These actin and myosin filaments partly interdigitate to form alternate dark and bright (light) bands.</p> <ul style="list-style-type: none"> ▪ I band is the light band containing only actin filaments and Isotropic to polarized light ▪ A band is the dark band having actin + myosin filaments where they overlap, Anisotropic to light ▪ H zone is the light area in center of A band seen upon muscle stretching ▪ M line is the dark line in the center of H zone ▪ Z line or disc passes from myofibrils to myofibrils attaching them together. Z lines defines the boundary of myofibrils and intersects I band. Actin attach to Z line through Actinin ▪ Sarcomere is the portion of myofibrils between 2 successive Z lines (i.e runs from Z-to-Z line) <p>Repeating units of sarcomere account for unique banding pattern in striated muscle</p> <table border="1"> <tr> <td>Thick Filaments</td><td> <ul style="list-style-type: none"> ❖ Present in A band in center of sarcomere and contains Myosin. ❖ Myosin has 6 polypeptide chains = 1 pair of heavy chain + 2 pairs of light chain ❖ Each Myosin molecule has 2 heads and 1 tail. ❖ Myosin heads bind ATP + actin and are involved in cross-bridge formation. </td></tr> <tr> <td>Thin Filaments</td><td> <ul style="list-style-type: none"> ❖ Present in I band and contain actin, tropomyosin, and troponin. ❖ anchored at Z- lines and interdigitate thick filaments in a portion of A band </td></tr> </table>	Thick Filaments	<ul style="list-style-type: none"> ❖ Present in A band in center of sarcomere and contains Myosin. ❖ Myosin has 6 polypeptide chains = 1 pair of heavy chain + 2 pairs of light chain ❖ Each Myosin molecule has 2 heads and 1 tail. ❖ Myosin heads bind ATP + actin and are involved in cross-bridge formation. 	Thin Filaments	<ul style="list-style-type: none"> ❖ Present in I band and contain actin, tropomyosin, and troponin. ❖ anchored at Z- lines and interdigitate thick filaments in a portion of A band
Thick Filaments	<ul style="list-style-type: none"> ❖ Present in A band in center of sarcomere and contains Myosin. ❖ Myosin has 6 polypeptide chains = 1 pair of heavy chain + 2 pairs of light chain ❖ Each Myosin molecule has 2 heads and 1 tail. ❖ Myosin heads bind ATP + actin and are involved in cross-bridge formation. 				
Thin Filaments	<ul style="list-style-type: none"> ❖ Present in I band and contain actin, tropomyosin, and troponin. ❖ anchored at Z- lines and interdigitate thick filaments in a portion of A band 				
Troponin	<p>A regulatory protein that permits cross-bridge formation when it binds Ca^{+2}.</p> <p>Troponin is a complex of three globular proteins:</p> <ul style="list-style-type: none"> ○ Troponin T ("T" for tropomyosin) attaches the troponin complex to tropomyosin. ○ Troponin I ("I" for inhibition) inhibits the interaction of actin and myosin. ○ Troponin C (C for Ca) is Ca²⁺-binding protein, when bound to Ca, permits the interaction of actin & myosin 				
T tubules	<ul style="list-style-type: none"> ▪ Extensive tubular network located at the junctions of A bands, and I bands ▪ T tubules conducts action potential from sarcolemmal membrane to interior of muscle fiber. ▪ They contain voltage-sensitive protein called the dihydropyridine receptor; depolarization causes a conformational change in the dihydropyridine receptor 				
Sarcoplasmic reticulum	<ul style="list-style-type: none"> ▪ SR is the internal tubular structure that is the site of Ca^{+2} storage and release for excitation-contraction coupling. ▪ It has terminal cisternae that make intimate contact with T tubules in a triad arrangement ▪ SR membrane has Ca^{+2}- ATPase (Ca pump), which transports Ca^{+2} from intracellular fluid into the SR interior, keeping intracellular $[\text{Ca}^{+2}]$ low. ▪ contains Ca^{+2} bound loosely to Calsequestrin. ▪ contains a Ca^{+2} release channel called the ryanodine receptor 				

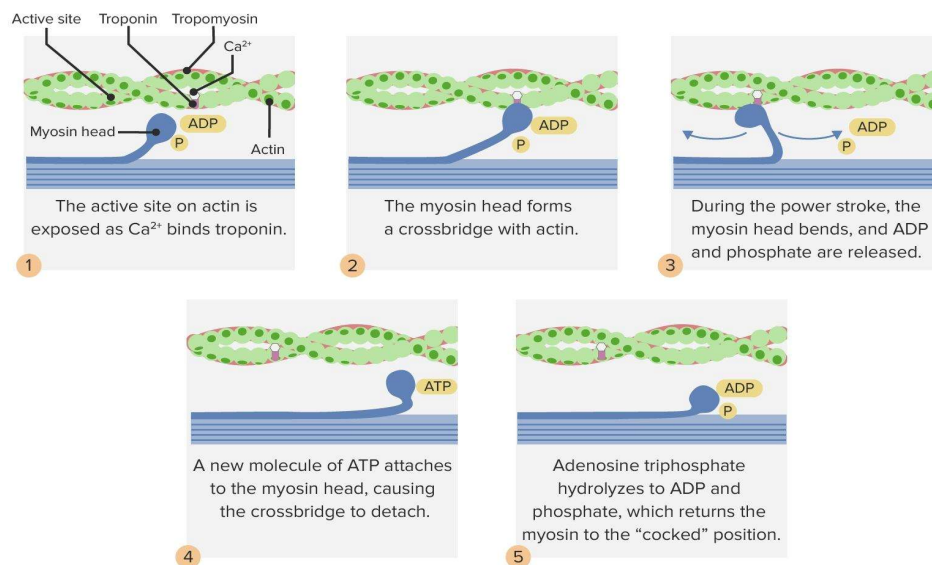


STEPS OF EXCITATION – CONTRACTION COUPLING IN SKELETAL MUSCLES

- Action potentials in the muscle cell membrane initiate depolarization of the T Tubules
- Depolarization of T Tubules causes release of Ca^{2+} from SR of into the Intracellular fluid. Intracellular Ca^{2+} increases
- Ca^{2+} binds troponin C on the thin filaments, causing a conformational change in troponin that moves tropomyosin out the way. The cross-bridge cycle begins.

Cross-bridge cycle

1. The myosin head is attached to the actin filament with ADP + Pi.
As we know, the myosin head is able to bind to the actin because once myosin-binding site is revealed once a calcium molecule binds to the troponin on the actin causing a conformational change that allows for the myosin-binding site to be revealed and for the myosin head to bind, Thus, calcium regulates muscle contraction
 2. Once the **myosin head binds, its “pivots” and a power-stroke is generated**, Myosin is displaced towards the plus end of actin. There is hydrolysis of ATP to ADP and inorganic phosphate (Pi).
- As new ATP attaches to the myosin head, Cross bridge detaches
ATP is necessary to release the myosin from the actin, which allows for the muscles to relax and then be ready to undergo another cycle of contraction and crossbridge forming.
 - ✓ **Contraction will produce no change in length of A band. I band and H zone shorten or reduced in size**
 - ✓ **In rigor mortis**, which is a condition that takes place soon after death, the body is no longer making ATP which is why the Muscles are incredibly stiff; the myosin heads are unable to detach from actin
 - ATP hydrolysis will then cause the myosin head to once again “cock” and be in the appropriate Conformation to be ready to bind to “myosin-binding site” on the actin filament once again. The ATP is now ADP + Pi.
The myosin head + ADP + Pi once again binds to the actin. The cycle begins (same as step 1)
- **The cycle repeats as long as Ca^{2+} is bound to troponin C.**
- Each cross-bridge cycle “walks” myosin further along the actin Filament.
- Relaxation occurs when Ca^{2+} is re-accumulated by the SR Ca^{2+} -ATPase (SERCA). Intracellular Ca^{2+} Concentration decreases, Ca^{2+} is released from troponin C, and tropomyosin again blocks the myosin- Binding site on actin
- As long as intracellular Ca^{2+} concentration is low, cross-bridge cycling cannot Occur



SMOOTH MUSCLES

- They have thick and thin filaments, not arranged in sarcomeres – therefore, they appear non-striated.
- Smooth muscle has inner circular and outer longitudinal layer
- Smooth muscles cause Slow sustained prolong contraction (low energy mechanism)

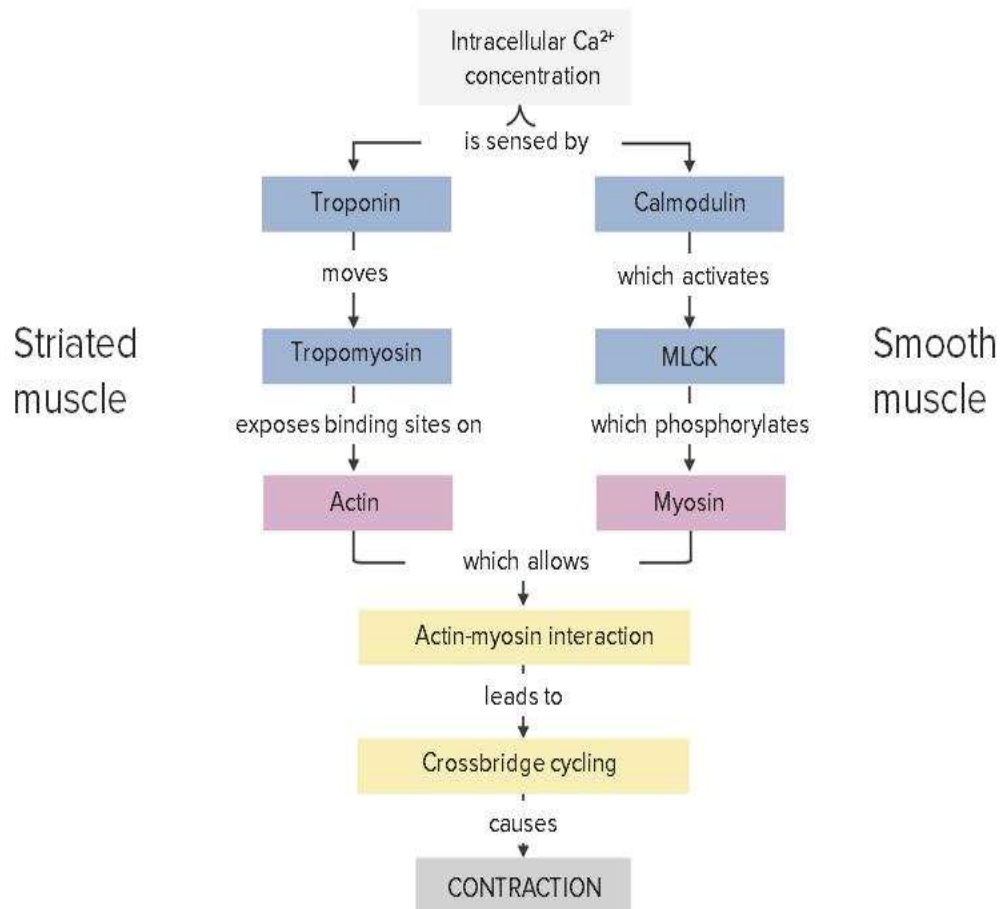
Types of Smooth muscles	Single unit or Unitary	Most common type, present in viscera – GIT , Genitourinary tract (uterus, ureter, bladder) They are spontaneously active, exhibit slow waves and pace-maker activity which is modulated by hormones and neurotransmitters.
	Multiunit	Behaves as separate motor units and densely innervated Has little or no electrical coupling between cells Located in iris, ciliary muscle of lens and vas deferens Contraction is controlled by neural innervation –autonomic nervous system
	Vascular	Has properties of multiunit and single unit smooth muscle.
Steps in Excitation-contraction coupling	<ul style="list-style-type: none"> ➤ There is no troponin; instead, Ca^{2+} regulates myosin on the thick filaments. ➤ Depolarization of the cell membrane opens voltage gated Ca^{2+} channels and Ca^{2+} flows into the cell down its electrochemical gradient increasing the intracellular $[\text{Ca}^{2+}]$. ➤ Hormones and neurotransmitters may open ligand- gated Ca^{2+} channels in cell membrane, Ca^{2+} entering the cell causes release of more Ca^{2+} from the SR in a process called Ca^{2+}-induced Ca^{2+} release. ➤ Hormones and neurotransmitters also directly release Ca^{2+} from the SR through inositol 1, 4, 5-trisphosphate (IP₃)-gated Ca^{2+} channels. ➤ Intracellular $[\text{Ca}^{2+}]$ increases and Ca^{2+} binds to calmodulin ➤ The Ca^{2+}-calmodulin complex binds to and activates myosin light chain kinase. ➤ When activated, myosin light chain kinase phosphorylates myosin and allows it to bind to actin, thus initiating cross-bridge cycling. ➤ The amount of tension produced is proportional to the intracellular Ca^{2+} concentration ➤ A decrease in intracellular $[\text{Ca}^{2+}]$ produces relaxation (Latch mechanism) 	

Summary

1 Cytosolic $\text{Ca}^{+2} \rightarrow \text{Ca}^{2+}$ - calmodulin \rightarrow activation of myosin kinase \rightarrow Phosphorylation of MLCK \rightarrow activation of myosin ATPase \rightarrow attachment of myosin head with actin \rightarrow contraction by sliding filament model

COMPARISON OF SKELETAL, CARDIAC AND SMOOTH MUSCLES

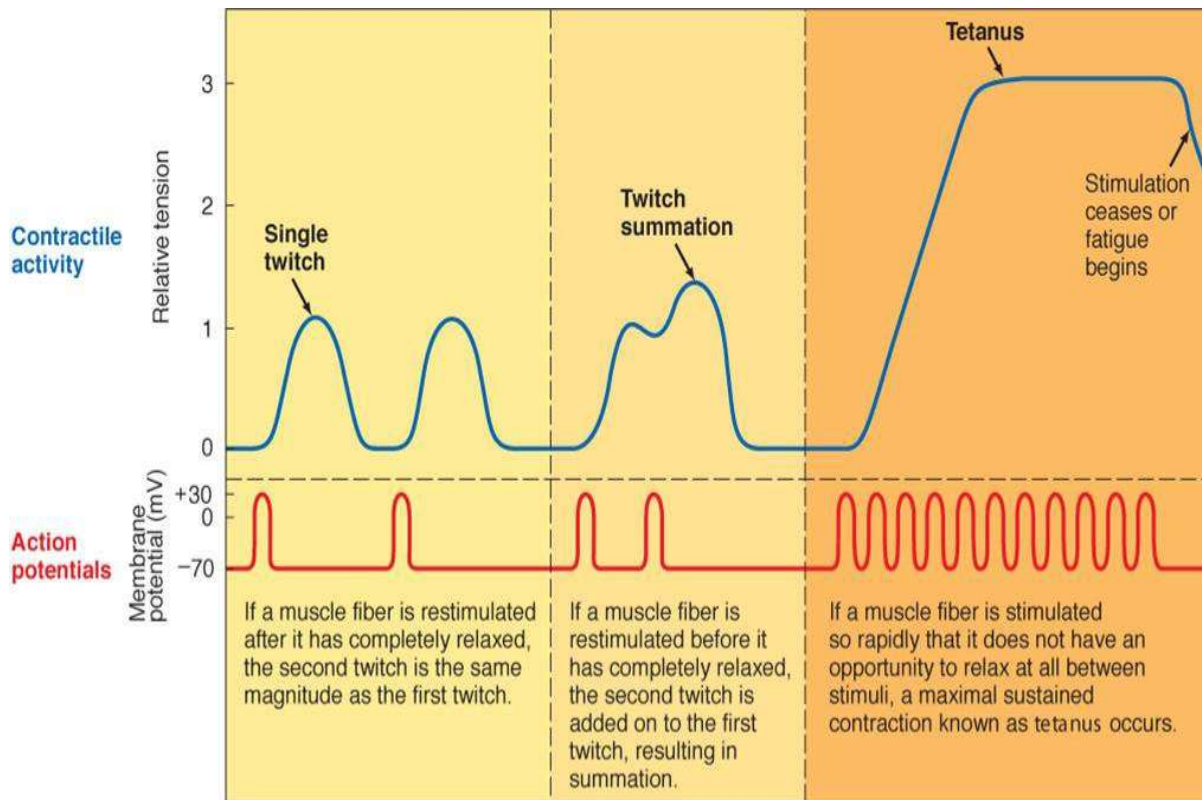
Type	Appearance	Structure	Arrangements	Upstroke Of AP	Contraction
Skeletal	Striated	Has T-tubules	Actin and myosin form sarcomere	By Inward Na^{+} current	Ca^{+} - troponin C
Cardiac	Striated	Has T-tubules	Actin and myosin form sarcomere	SA node: inward Ca^{+2} Atria, vent, Purkinji: Inward Na^{+} current	Ca^{+} - troponin C
Smooth	Non-Striated	Lacks T-tubules	Not arranged in sarcomeres	Inward Ca^{+2} current	Ca^{+2} calmodulin



KEY FACTS

- Plateau is present in cardiac muscles action potential (atria, ventricles, purkinji) due to inward Ca^{+2} current or influx of Ca^{+2} and efflux of K^{+} ions
- Duration of action potential is 1 msec in skeletal muscle, 10 msec in smooth muscles, 150 msec (SA node, atria) and 250 msec in ventricles + purkinji fibers
- Intercalated discs present in cardiac muscles, and they maintain cell-cell cohesion
- Skeletal muscle has multiple peripheral nuclei while smooth and cardiac have single central nucleus
- Automaticity/Rhythmicity is a feature of cardiac muscle, absent in smooth and skeletal muscles
- Cardiac muscle don't get tetanized because of long refractory period
- Common muscle contraction protein for Smooth muscle and skeletal muscle is Actin
- Common feature between smooth and skeletal muscle is Increased intracellular Ca before contraction
- Common feature between cardiac and skeletal muscle = Transverse striation
- Difference between Skeletal and smooth muscle = Ca Calmodulin complex in Smooth muscle
- SR is the Ca^{+2} source in skeletal + cardiac muscles while;
- Extracellular Ca^{+2} is the Ca^{+2} source in smooth muscles
- Continuous contraction without relaxation period is called Tetanus
- Continuous contraction with a relaxation period in between contraction is called Tetany
- Latent tetany is seen in Conn's syndrome

- Titin is the largest known protein that Stabilizes the position of contractile filaments Functions as a molecular spring, which is responsible for the passive elasticity of muscle. It connects the Z line to the M line in the sarcomere
- Titin is the third most abundant protein in the muscle (after myosin and actin)
- Titin is the largest known protein. Actin is the most abundant protein in most eukaryotic cells.
- Collagen is the most abundant protein in the body, making 25-35% of all the whole-body Proteins
- Dystrophin gene (DMD), is the longest known human gene



Isotonic contraction	Shortening of muscle Length with no change in tension, more energy is used as external work is done. Example: Exercising in gym, lifting a cup of tea to the mouth Isotonic contraction is best for improving muscle strength
Isometric contraction	Length remains same while tension increases, less energy is used due to less or no work done. Example: A man pushing against a wall

HEAT CHANGING MECHANISMS DURING MUSCLE CONTRACTION

Resting Heat	Heat produced in muscle at rest due to basal metabolic process						
Initial Heat	During muscle contraction , heat production in excess of resting heat, occurs in 3 stages: <table border="1"> <tr> <td>Heat of Activation</td><td>Also called maintenance heat, produced before actual shortening of muscle during the release of calcium ions from L tubules (Longitudinal)</td></tr> <tr> <td>Heat of Shortening</td><td>Heat produced during muscle contraction due to structural changes (shorten)</td></tr> <tr> <td>Heat of Relaxation</td><td>Heat released during muscle relaxation and produced due to breakdown of ATP during muscle contraction</td></tr> </table>	Heat of Activation	Also called maintenance heat, produced before actual shortening of muscle during the release of calcium ions from L tubules (Longitudinal)	Heat of Shortening	Heat produced during muscle contraction due to structural changes (shorten)	Heat of Relaxation	Heat released during muscle relaxation and produced due to breakdown of ATP during muscle contraction
Heat of Activation	Also called maintenance heat, produced before actual shortening of muscle during the release of calcium ions from L tubules (Longitudinal)						
Heat of Shortening	Heat produced during muscle contraction due to structural changes (shorten)						
Heat of Relaxation	Heat released during muscle relaxation and produced due to breakdown of ATP during muscle contraction						
Recovery Heat	Heat produced after the end of activity due to chemical processes involved in resynthesis of chemical substances broken down during contraction. Recovery heat is equal to initial heat.						

Type 1 (Red or slow twitch muscle fibers)	Type 2 (White or fast twitch muscle fibers)
<ul style="list-style-type: none"> More myoglobin (red color), smaller fiber length More mitochondria – aerobic metabolism Extensive blood supply, fatigued late Myosin ATPase is slow (Slow and prolonged action) Examples: Soleus, gluteal muscles, back muscles 	<ul style="list-style-type: none"> Less myoglobin (white color), larger fiber length Less mitochondria – anaerobic metabolism Less extensive blood supply, early fatigue occurs Myosin ATPase is fast (Quick and precise) Gastrocnemius, biceps brachii, extraocular muscles
Positive Feedback mechanism	Output exaggerate the original stimulus, also called a vicious cycle because once started may lead to the death. Example: Blood clotting, Childbirth (action of Oxytocin on uterus), LH surge
Negative Feedback mechanism	When the result is opposite to initial stimulus, it is called the negative feedback. The most human system achieves homeostasis by Negative feedback mechanism. Examples: Body Temperature, blood glucose level, Blood PH, Blood pressure , Hormone level, Oxygen and Carbon-dioxide level , water and electrolyte balance etc. are all controlled by negative Feedback. Other examples: Baroreceptor reflex, Renshaw cell (lateral inhibition)

Heat Cramps	They occur when the body's levels of salt and moisture are depleted, aka excessive sweating. Symptoms include Muscle cramps, Pain or Spasms in the abdomen, arms, or legs. First Aid: Stop All Activity, sit in a cool area, go under shade, Drink clear juice, a sports beverage, or water with food. Avoid salt tablets and don't return to work for few hours after cramping subsides.
Heat Pyrexia	Fever: Change in hypothalamic set point, involves cytokines, and rarely temp exceeds 41 C Hyperthermia: Failure in Thermoregulation, can exceed > 41 C, Absence of diurnal variations
Heat Exhaustion	Heat Exhaustion is the body's response to an excessive loss of water and salt, usually through sweating. Symptoms: Heat Cramps, Rapid Heartbeat, Heavy Sweating , Extreme Weakness, dizziness Nausea, Vomiting, Irritability, Fast Shallow Breathing and Slightly Elevated Body temperature First Aid: Stop all activity, Rest in a cool area, Drink plenty of cool beverages, Take a cool shower, bath or sponge bath, do not return to work for the day Medical Attention Should Be Sought If Symptoms Worsen or Do Not Improve In 1 Hour
Heat Stroke	Heat Stroke is the most serious heat-related illness and can lead to permanent damage or death. It occurs when the body loses control of regulating its temperature. Symptoms: High Body Temperature > 103 C , Confusion, Lack of Coordination, Hot and Dry Skin , Profuse Sweating, Rapid Heartbeat and Breathing, Throbbing Headache, Fainting, Seizures and Coma First Aid <ul style="list-style-type: none"> Call for help (1122) and seek medical assistance immediately Move worker into a cool shaded area. Remove any excessive clothing, Try to cool their body down by applying cool water to their body, covering them with cool wet towels, applying ice to their armpits, neck, and wrists. Stay with the victim until help arrives Do not force the victim to drink liquids or allow them to take pain killers or salt tablets. Medical attention should always be sought

MECHANISM OF HEAT ENERGY TRANSFER & HEAT LOSS TO ENVIRONMENT	
<ul style="list-style-type: none"> Four mechanisms for heat transfer: Radiation, conduction, convection, evaporation Heat loss depends upon core body temperature 	
Radiation	<ul style="list-style-type: none"> Energy transferred by Electromagnetic Waves such as light, Microwaves, and Infrared radiation. All objects radiate Energy. Radiation can transfer energy through empty space and does not involve the movement of matter
Convection	<ul style="list-style-type: none"> Convection is the transfer of heat energy by the movement of fluids(gas or liquid) Occurs due to Difference in density. Cycle occurs while Temperature Differences exist Convection currents due to hot fluid rising and Cold fluid sinking Occurs in gases and Liquids by Movement of large Number of particles In same direction
Conduction	<ul style="list-style-type: none"> Conduction is the transfer of heat energy by Between particles of objects in direct contact. Energy flows directly from warmer object to cooler object. It can occur within one Object and Continues until object Temperatures are Equal
Evaporation	<ul style="list-style-type: none"> Evaporation is the transfer of heat by the evaporation of water, takes a great deal of energy for a water molecule to change from a liquid to a gas, evaporating water (in the form of sweat)

KEY FACTS – HEAT LOSS

- Person or object is naked, heat loss occurs via = radiation
- Person is naked and lying (contact with table or OT table), heat is lost via = Conduction
- Person is naked at for example 23C (**temperature mentioned**), heat loss by = radiation + conduction
- Patient is naked and **humidity** mentioned, heat loss by = Convection
- Convection requires medium (medium is humidity here)
- if tracheostomy or ETT mentioned, heat loss via = Evaporation
- A Person naked at temp 18C, humidity 65%, heat loss via = **Radiation + conduction + convection** > Radiation + Conduction

TOTAL BODY WATER (TBW)

- TBW is 60% of body weight. For example, in a 70kg man the TBW is 42 Litre
- TBW is divided into Extracellular fluid + intracellular fluid.
- Remember the rule 60 – 20 – 40**
- TBW** is 60% of body weight, **ICF** is 40% of body weight, **ECF** is 20% of body weight.
So, in 70 kg male; TBW = 70×0.6 (60% body weight) = 42 Litre
ICF = 70×0.4 = 28 Litre while ECF = 70×0.2 = 14 Litre

Extracellular Fluid (ECF, 14L)

1/3rd Of Total Body Water Present in Spaces Outside The Cell
Contains Nutrients and Ions Essential for Cell Life, also called Internal Environment of Body.

- Major Cations** = Na⁺
- Major Anions** = Cl and HCO₃
- ECF Further Divided Into plasma and interstitial fluid**
- Transcellular fluid** is the portion of TBW contained within epithelial lined spaces. It is the smallest component of extracellular fluid and often not calculated as a fraction of ECF, but it is about 2.5% of the total body water.

Plasma 1/4th of ECF or 1/12th of TBW, Present in Blood- Contains Plasma Proteins
Plasma volume = 3.5 Liter (20% of TBW)

Interstitial fluid 3/4th of ECF, present in space between cells, has low protein as compared to plasma.
Interstitial fluid volume = 10.5 - 11 Liter

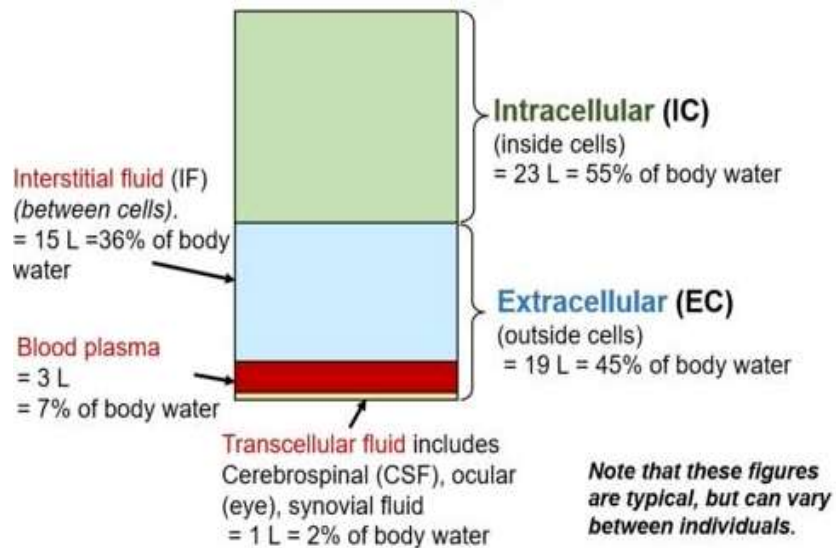
Intracellular Fluid (ICF, 28L)

2/3rd of TBW, contains large amount of K⁺, Mg⁺² and Phosphate ions, slightly **acidic** to ECF

Major cations = K⁺, Mg⁺² (98% K is inside the cells or intracellular)

Major Anions = Proteins

Cells are bags of Potassium (more K⁺ inside) floating in a Sea of sodium (more Na⁺ outside)



PAST PAPERS BCQs

1. Abundant in cell membrane = Proteins (55%). Highest component in Lipid is of = Carbon
2. Phospholipids have = both polar and non-polar ends
3. Event that happens at NMJ = Ca^{+2} uptake in presynaptic terminal, release of acetylcholine (ACh)
4. A man with myasthenia gravis notes inc muscle strength when given Pyridostigmine (AChE inhibitor). The cause for this = increased levels of ACh at motor end plate (remember, the ACh receptors density reduces in myasthenia)
5. During upstroke of action potential = there is net inward movement and cell interior becomes less -Ve
6. Subsequent action potentials can = Summate (Temporal summation)
7. All or none action potential is initiated at = Axon hillock, AP first generated at Axon hillock
8. Initiation of AP requires = release of ACh
9. During refractory period = a 2 nd AP cannot occur despite the stimulus (especially in absolute refractory period)
10. Conduction of one type of sensation modality at a time is = Labelled line principle
11. Inactivation Na gates are closed during = Depolarization
12. Secondary active transport requires = Carrier, uses energy of Na^{+} , ATP not directly used
13. Transport of solute in active transport requires = Energy in the form of ATP
14. Cyclic AMP (Camp) formation involves = Enzyme , Camp involves = Receptor (for formation – enzyme)
15. Resting membrane potential achieved by = K^{+} efflux, (maintained by Na, K^{+} ATPase pump)
16. Hyperpolarization of nerve fiber is due to = K^{+} efflux. Plateau phase of AP depends on = Ca^{+} influx, K^{+} efflux
17. IV potassium given to a patient, it will enter cell via = Na, K^{+} pump
18. Extracellular and intracellular K^{+} maintained by = Na, K^{+} pump
19. Hyponatremia decreases = height of Action potential. Conduction is not possible in = Hyponatremia
20. Decreased height of AP with flat or low T wave = Hypokalemia (T waves changes correspond to K^{+})
21. Hypercalcemia decreases the membrane excitability
22. Increased neuronal excitability at RMP = Hyperkalemia
23. Na, K^{+} ATPase inhibition causes = raised intracellular Ca^{+2} -- mechanism of action of digoxin
24. Hyperexcitability of neurons due to low levels of = Ca^{+2}
25. What works through sympathetic rather than local metabolite = Skin
26. Constant depolarization of axonal membrane depends on = Capacitance or conductance of membrane to ions
27. Action potential transfers from cell to cell by = Gap junctions (for chemical and electrical exchange)
28. Structure connecting 2 epithelial cells only = Tight junctions
29. Cells of simple columnar epithelium are connected by = Tight junctions
30. Connections between cells that prevent passage of materials = Tight junctions
31. Cells of simple columnar epithelium connected to each other by = Tight junction, adherent junction, and desmosome
32. Structure that is like spot weld between 2 epithelial cells = Desmosomes
33. Connected to desmosomes are = Intermediate filaments
34. Responsible for adhesion during embryonic development belonging to CAM family = Cadherins

35. Bonds in cell membrane = Hydrogen + Hydrophobic > Hydrophobic + covalent
36. Integral proteins are joined to lipid of membrane by Hydrophobic bond > hydrophobic + covalent bond
37. Maximum permeability of cell membrane is to = Water. Water enters cell via = Pores
38. Water has high diffusion capacity than Na, K, K and glucose
39. Haematoxylin stains nucleus = Blue. On H & E, Hollow structure around nucleus = Lysosomes
40. Gap junctions present in Cardiac + smooth muscles, absent in skeletal muscles
41. Osmosis depends upon = No. Of solute particles. Choline is component of = Sphingomyelin
42. Function of cholesterol in membrane = maintains fluidity + permits ions movement
43. Basement membrane has -Ve charge due to = Heparin sulfate > Laminin
44. Assessment of muscle injury done by = CKMM.
45. Stimulation of nerve trunk generates = Compound action potential
46. Diplotene stage seen in = Prophase, chromosomes are paired in = Prophase
47. Chromosomes at equatorial plate, thickest and best studied at = Metaphase
48. Self-replicating organelle = mitochondria, having own DNA – maternally transmitted.
49. Generation of free radicals by = mitochondria
50. Oxidation of very long chain FA = Peroxisomes, for short chain FA = mitochondria
51. Alcohol detoxification occurs by = Peroxisomes (at normal dose)
52. Lysosomes have = Hydrolytic enzymes. Peroxisomes have = Oxidase, catalase, H ₂ O ₂
53. Peroxisomes originate from SER. Lysosome originate from Golgi complex
54. Similarity b/w cardiac and smooth muscles = Mononucleated, while skeletal muscles = Multinucleated
55. Cross bridges formed by = Myosin head (power stroke). A band has = Myosin + some actin
56. Rigidity after death or Rigor mortis due to = Failure of separation of myosin actin crosses bridges due to low ATP.
57. Unchanged in muscle contraction = A band. Shortening occur of = I band + H zone
58. Sarcomere is seen b/w = 2 Z lines. contractile unit of skeletal muscles = sarcomere
59. Actin is bound to Z line via = Actinin. Common contractile protein b/w striated muscles = Actin
60. Transverse striations present in = cardiac and skeletal muscles
61. Tetany is not seen in = Cardiac muscles due to long refractory period
62. Continuous contraction without relaxation = Tetany
63. Longest phase of cell cycle = G ₁ phase (8-10 hrs). Shortest phase = M phase
64. Phase affected most by chemotherapy = S phase. Radiotherapy affects = M > G ₂ phase
65. Glycocalyx contains Carbs (glucose) present on = Outer surface of membrane
66. Flow through medium depends on = Viscosity. Flow through orifice depends on = Density (OD)
67. Basal bodies formed by = centrioles. Basal body forms = Cilia + Flagella
68. D and L glucose are transported by = Co-transport
69. D and L glucose are transported down electrochemical gradient via = Simple diffusion
70. Glucose transport in placenta by = Facilitated diffusion. Facilitated diffusion has = V _{max}
71. Local anaesthesia crosses placenta by = simple diffusion. Thickness of membrane affects = Diffusion
72. CO ₂ transports via = Simple diffusion (passive process) O ₂ transport in lungs by = Simple diffusion.
73. Nissle substance consist of = RER in neurons
74. Maximum transport maximum is seen with = Glucose. GPL (Glucose > PAH > Lactate)
75. Type of endocytosis in lysosomes = Phagocytosis
76. Double membrane bounded organelles = Nucleus + mitochondria
77. Skeletal muscles have = fleshy belly throughout. Origin is immobile while insertion is mobile.
78. During prolonged surgery temperature of patient is monitored by = Probe in Esophagus
79. Cells with basal infolding on microscope have = Villi – increase the surface area for absorption
80. PCT has abundant Microvilli (brush border) than DCT. Abundant cilia seen in = Maxillary sinus > Fallopian tube
81. Increased mitochondria present in = Ciliated cells > cardiac cells
82. Skeletal muscles respond to trauma by = Increased proteolysis
83. Drug receptor nature = Protein.
84. Euchromatin is = Lightly condensed and active DNA
85. Actively dividing cells have = prominent nucleoli (basophilic)
86. Fibroblasts produce fibrosis and granulomas
87. Decreased DNA and cell activity seen in = Cell aging process
88. DO not regenerate = Permanent cells (skeletal > cardiac cells). Diffusion is directly to = Surface area

89. Growth factors receptors present on = plasma membrane
90. Centrioles composed of = Microtubules. Epithelial cell marker = Cytokeratin. Muscle marker = desmin
91. Fructose transport in GIT via = Facilitated diffusion
92. Calcium in skeletal muscles bound to = Calsequestrin. No troponin seen in = Smooth muscles.
93. Smooth muscles lack T tubules. preferential thoroughfare channels have = Smooth muscles
94. Dartos fascia has = Smooth muscle. Heart cells have no potential for division
95. Drug detoxification is via = SER
96. Malignant hyperthermia is due to = Ryanodine receptors
97. Heat generates in Malignant hyperthermia via = Skeletal muscle contraction
98. Side effect of Succinyl choline = Malignant hyperthermia
99. Clearance of defective protein by = Proteosomes
100. Protein misfolding prevented by = Chaperons
101. G protein phospholipase C and IP ₃ , DAG increase = Ca^{+2} intracellularly
102. Sustained contraction of skeletal muscle with a relaxation period during contractions is = Tetanus
103. Accumulation of which solute is responsible for tetanus = ATP (ATP levels eventually fall due to sustained contraction)
104. Similarity between simple and facilitated diffusion = occur down the electrochemical gradient
105. Solutions A and B separated by a semi-permeable membrane that is permeable to K ⁺ only. Solution A has 10 mM KCL and solution B has 2 mM KCL. What will happen = K ⁺ will diffuse from higher (solution A) to lower (solution B) until a membrane potential develops with solution A -Ve with respect to solution B
106. Similarity b/w skeletal and smooth muscle excitation contraction coupling = Ca^{+2} raised intracellularly in both
107. A male infused with a solution that caused lysis of cells (RBCs), the solution may be of = 300 mM Urea (hypotonic)
108. RBC kept in hypertonic solution containing urea what will happen = transiently Shrinks, then swells and lyses Explanation: Water will come out of RBC first due to higher tonicity outside, later both urea + water diffuse in and let cell swell, later lyses
109. Rbcs is kept into urea solution what will happen = Swell and Lyse (as, urea solution is hypotonic)
110. RBC kept in hypotonic urea solution will = swell and lyse (ruptured)
111. old man with oat cell carcinoma of lung diagnosed him with (SIADH) and treated him immediately with
112. Hypertonic saline to prevent another seizure. Which of the following is the most likely
113. Value of the man's plasma osmolarity before Treatment = 235 mOsm/L
114. In SIADH (osmolarity less than 280) while in water deprivation Osm > 280 mOsm/L
115. Difference of plasma and interstitial fluid Osmolarity = 1 mOsm/Lit
116. 1mM CaCl ₂ is hypertonic or would be hyperosmotic to 1 mM NaCl
117. A new drug is developed that blocks the Transporter for H ⁺ secretion in gastric parietal cells. Which of the following transport Processes is being inhibited = Primary active transport
118. old woman with severe muscle Weakness is hospitalized. The only abnormality in her laboratory values is an elevated Serum K ⁺ concentration. The elevated serum K causes muscle weakness because = Na ⁺ channels are closed by depolarization. Sustained depolarization causes opening of inactivation gates of Na ⁺
119. In contraction of gastrointestinal smooth Muscle, which of the following events occurs After binding of Ca^{+2} to calmodulin = Increased myosin light chain kinase
120. Which of the following transport processes is involved if transport of glucose from the intestinal lumen into a small intestinal cell is inhibited by abolishing the Usual Na ⁺ gradient across the cell membrane = Cotransport
121. In skeletal muscle, which of the following Events occurs before depolarization of the T tubules in the mechanism of excitation-Contraction coupling = Depolarization of the sarcolemmal Membrane
122. Which of the following is an inhibitory Neurotransmitter in the (CNS) = γ -Aminobutyric acid
123. (ATP) is used indirectly for = Absorption of glucose by intestinal Epithelial cells (2° active transport)
124. A newly developed local anaesthetic Blocks Na channels in nerves.
125. Which of the following effects on the action potential Would it be expected to produce = Decrease the rate of rise of the upstroke of the action potential
126. At the muscle end plate, acetylcholine (Ach) causes the opening of = Na ⁺ and K channels and depolarization
127. To a value halfway between the Na ⁺ and K ⁺ equilibrium potentials
128. An inhibitory postsynaptic potential = hyperpolarizes the postsynaptic membrane by opening Cl channels
129. Following temporal Sequences is correct for excitation-Contraction coupling in skeletal muscle = Action potential in the muscle membrane → depolarization of the T tubules → Release of Ca ⁺ from the SR
130. Childbirth and blood clotting examples of = +Ve feedback mechanism
131. Homeostatic function of autonomic system is opposed in = -Ve feedback system

132.CSF is example of = Transcellular fluid
133.Steady environment in body due to = -Ve feedback.
134.High in tears than plasma = Amino acids
135.Nucleolus has = No limiting membrane. Thickness of cell membrane = 7.5 nm
136.Protein synthesis occurs in = Ribosomes > RER. Major content of nucleolus = r RNA large collection
137.Axoneme of cilia has = 20 microtubules. Defect in Kartagener syndrome = Dynein arm
138.Lipid bilayer is soluble for = CO ₂ . Wound healing promoted via = Microfilaments (actin)
139.ECM is connected to ICM by = Intermediate filaments
140.Force generating proteins = dynein and kinesin
141.Non energy consuming process = diffusion of gases
142.58 mg of NaCl dissolved in 1 Lit solution has osmolarity = 2
143.While calculating plasma Osmolality. Na is multiplied by 2 = Anions
144.Osmolarity of 8.4% NaHCO ₃ = 2000 mOsm/kg. Explanation: NaHCO ₃ osmolarity = 1 Na + 1 Hco ₃ → 2 Osm/kg. Multiply by 1000 to convert Osm to mOsm = 2000
145.Membrane protein Clathrin is involved in = receptor mediated endocytosis
146.Movement of molecules across membrane occurs via = Fick's law
147.Na is transported across basolateral membrane by = Na, K-ATPase
148.Calmodulin is like = Troponin C .
149.Heart works as a syncytium due to = Gap junctions
150.Absolute refractory period of heart = 200 m sec
151.Intercalated disc present in = cardiac muscles only – maintain cell to cell cohesion
152.AP of skeletal muscles = spreads inward to all parts via T tubules
153.Electrotonic potential = Dec threshold for AP
154.Neuronal excitability is caused by = Hypocalcemia and alkalosis

CARDIOVASCULAR SYSTEM

CARDIAC OUTPUT (SV × HR)

- Amount of blood pumped by each Ventricle/min.
- CO of Left Heart (systemic Blood flow) equals CO of Right Heart (Pulmonary blood flow)
- CO = Stroke Vol (70ml) × Heart Rate (70-72 beats /min) → 5 Lit/Min Normal.
- Max CO received by → Liver > kidney > brain > heart > skin.
- CO ↑ After Delivery of baby (BCQ)
- Fick principle (most accurate for CO measurement but invasive) states as:
CO = Rate of O₂ consumption ÷ (Arterial O₂ content-Venous O₂ Content)
- O₂ consumption is 250 ml/min.
- O₂ consumption inc by **inc Heart size**, contractility, heart rate and afterload.
- CO can also be measured by **Thermodilution** also called Indicator dilution method (BCQ) which uses
- Cardio green/indocyanine dye measured in Aorta Wheatstone bridge also used to find CO.
- 60 to 70% energy provided by FATS (BCQ) and Rest by Glucose & Lactate.
- CO is Unchanged in Sleep.
- While CO inc in Exercise (highest 700% inc) > Anxiety/excitement > Eating and pregnancy
- Dec CO in standing/sitting from lying, Dec Skeletal muscle mass and heart diseases.
- Major determinant of CO is **Venous Return** (VR is flow of blood from systemic Veins towards Heart) As stated by Frank Starling Law which explains inc CO when VR is inc (BCQ) as circulatory system is a closed-Circuit system.

CO = VR or CO directly proportional to VR (BCQ)

Imp Concepts:

- ✚ Main determinant of VR Or VR to Rt Atrium is Mean systemic filling pressure (MSFP) 7mmHg (which is measured when VR is zero by stopping heart so that pressure everywhere in circulation is equal.
- ✚ So, at MSFP, VR=0 (All circulatory responses are abolished /Circulation Stops (imp BCQ))
- ✚ VR is inc by Skeletal Muscle contraction in Legs (soleus pump/2nd heart) as in Exercise.
- ✚ Athletes have high Resting CO & inc Stroke vol but Dec Heart rate (imp BCQ)
- ✚ So, in Athletes HR is < 60/min --- called physiological Bradycardia (not abnormal)

Variables Linked to Cardiac Output

Stroke Volume	<p>Vol. of Blood Pumped out of Left Ventricle during each Systolic contraction. SV is 70ml approx. SV = (End diastolic Vol - End systolic Vol)</p> <p>Tip: in EDV-ESV, remember D (as in EDV) comes before S (as in ESV) - remember it like this.</p> <p>SV = CO/HR. ↑ HR leads to ↓ SV</p> <p>End Diastolic Vol (120ml): amount of blood in Ventricles before heart contraction.</p> <p>End Systolic Vol: (50ml) amount of blood in heart after Contraction/Systole or you can say at beginning of diastole(filling). it is lowest Vol at any phase of Cardiac Cycle.</p> <p>SV ∝ EDV/ESV</p> <p>↑ SV will ↓ ESV(BCQ) SV ↑ with increased Contractility(exercise) & inc Pre-Load whereas inversely to Afterload Which means inc Blood Vol ↑ SV (BCQ)</p>
Contractility	<p>inc/dec by B1 receptors stimulation & inhibition via Catecholamine & Beta blockers respectively. Parasympathetics Dec HR.</p> <p>Digoxin blocks NA/K Pump → Inc intracellular Na → Dec Na/Ca exchanger & ↑ intracellular Ca²⁺</p>

Pre-Load & Afterload	Pre-Load	Afterload
	<ul style="list-style-type: none"> Amount of the blood heart receives. So, preload is a Stretch. Determined by End diastolic Volume (EDV). Related to Rt Atrial pressure. So, CO is a function of EDV, but CO is determined by (or) dependant on VR. Preload is an imp indicator of Left Ventricular End diastolic Vol (LV EDV). LV EDV > LV EDP Inc Pre Load leads to ↑SV (↑ EDV) 	<ul style="list-style-type: none"> The Pressure/Resistance Heart must Overcome to open aortic valve and eject the Blood. Stress is inversely to wall thickness. Preload is Stretch, but Afterload is Squeeze. ↑ Afterload leads to ↓SV(↑ ESV) Main Determinant of SV Is Afterload. Velocity of contraction at fixed muscle length is ↑ by ↓ afterload.
	<p align="center">Drugs that Dec Preload and Afterload (BCQ)</p> <p>Dec PrEload by Venodilators → Nitrates</p> <p>Dec Afterload by Arteriodilators (A in both Afterload & Arteriodil) → Hydralazine + Minoxidil</p> <p>Mixed (dec Both pre and afterload): ACE inhibitors & ARBs, Ca blockers are mixed type</p>	
Ejection Fraction	<ul style="list-style-type: none"> 55- 65%Normal EF= SV/EDV (BCQ) (OR) EF= EDV-ESV/EDV EF is Index of Ventricular contractility. EF dec in Systolic Heart failure while Normal in diastolic HF. Remember: EF is FRACTION of EDV ejected/beat, While AMOUNT of EDV ejected is SV (70ml). 	
Pulse Pressure	<ul style="list-style-type: none"> PP = (systolic B.P - Diastolic B.P) → PP = SBP (120 mmHg) – DBP (80 mmHg) = 40 Normal. PP is Directly ∝ SV and inversely to arterial compliance. Inc PP by Aortic Regurge, anemia, hyperthyroidism and HTN Dec PP by aortic stenosis (BCQ), Cardiac failure, Shock, and cardiac Tamponade. 	
Mean Arterial Pressure (MAP)	<ul style="list-style-type: none"> MAP = CO × TPR MAP = DBP + 1/3 PP (Or) 2/3 DBP+1/3rd SBP. MAP maintains blood flow to tissues -- major circulatory drive for blood flow (BCQ) Baroreceptors Determine MAP Best index of MAP is TPR > Afterload. While Afterload determined by MAP. Hypertension inc MAP → LV compensates for inc Afterload by inc Thickness/Hypertension which reduces wall tension. 	
Summary	<ul style="list-style-type: none"> ❖ CO = SV ×HR or CO = (EDV - ESV) × HR; (as SV = EDV – ESV) ❖ SV is directly to PP and MAP. ❖ CO is a function of EDV (preload) ❖ ↑ Preload increases SV + EDV (Inc Venous Return) ❖ ↑ Afterload inc ESV (Inc ESV → Decreases Stroke Vol) ❖ Main Determinant of CO is VR while determinant of VR is Mean systemic Filling Pressure ❖ MSFP can be determined from VR. ❖ Major Determinant of Stroke Vol is afterload. ❖ inc SV will ↓ ESV not EDV. ❖ Afterload determined/approximated by MAP (mean arterial Pressure). ❖ Work performed by Lt ventricle is greater than rt ventricle because afterload is greater in Lt ventricle (imp BCQ) ❖ Venous Return has no effect on pulmonary pressure. ❖ Force of contraction is directly to End diastolic length of cardiac muscle fibre (preload) explained by Frank starling Law. ❖ Best index of MAP is TPR > Afterload. ❖ Amount of EDV ejected is SV while fraction of EDV ejected is EF. ❖ During early exercise CO is maintained by inc SV & HR. while in late stage of exercise only HR increases. ❖ ↑ HR leads to ↓ SV but ↑ SV leads to dec. ESV. ❖ best indicator of vitals organ perfusion is MAP > Systolic B.P ❖ Myocardial O2 demand / Consumption inc by inc Heart size + HR and afterload. 	

	<ul style="list-style-type: none"> ❖ Cardiac Index is CO/body surface area. Normal is 2.8-3.2L/min/m². ❖ Heart Muscles Property = 80% O₂ consumption at Rest ❖ Inc Rt atrial Pressure leads to Inc HR. ❖ Highest Systolic Pressure in = Renal artery ❖ Max Pulse pressure: Dorsalis Pedis artery > femoral > Popliteal > Aorta
--	--

VASCULATURE

- Vessels are formed by 3 Layers: Tunica Adventitia (Outermost) Middle tunica Media & Inner Intima. (BCQ)
- Arteries are under high Pressure and blood in them is called Stressed Volume
- Veins are under low pressure having Unstressed Volume (64% of blood Vol.)
- Alpha1 receptors on Veins and arterioles of skin, splanchnic and Renal circulation.
- Beta 2 rec on arterioles of skeletal muscles
- Capillaries have highest total Cross sectional and Surface area (site of exchange of gases and nutrients but no innervation). They have Minimum diameter and blood flow velocity.
- **Arterioles are site of Highest Resistance/TPR**
- veins have highest blood vol/capacitance (v for veins & volume).
- Distribution of blood flow and Resistance mainly Regulated by Arterioles. (BCQ)
- Aorta has highest Pressure (100mmHg) and blood flow as well as Max wall thickness but minimum Cross-sectional area.
- Vena cava has Lowest pressure (4mmHg) but max diameter and blood Flow rate.
- **Blood flows from High pressure to Low pressure. Normal blood flow is 5L/min.**
- $P = Q \times R$ (remember it by PQR), $Q = P/R$. P is the pressure gradient that drives blood flow.
- Arm to brain circulation time is (10-20sec). Arm-Tongue is 15sec Arm to Foot is 21-30 sec.
- Laminar flow is steady and streamlined while Turbulent is in all directions like crosswise which creates Murmurs. **Reynold No. is the tendency of turbulence.**
- **Turbulence** increases by inc R No. to 2000 OR ↑ Diameter/Velocity and ↓ viscosity. (BCQ)
- Viscosity depends on Haematocrit.
- For increased turbulence: prefer inc Diameter > Dec Viscosity(BCQ)

Resistance (R)	Capacitance (Compliance)
<p>R is Directly to Length of vessel and Viscosity of blood but inversely to fourth power of radius of vessel.</p> <p style="text-align: center;">$R = 1/r^4$</p> <p>If Radius is halved (1/2) then R ↑ 16times (Imp BCQ)</p> <p>Shear is force/Stress of flowing blood on vessel, inversely to velocity.</p> <p>In wall of Vessel, velocity is Zero because shear is highest, whereas Velocity is Max in center of vessel as the shear is zero at the center.</p> <p>R in systemic Circulation is in Series $R(\text{total}) = R_1 + R_2 + R_3 + \dots$ while parallel in Organ system $1/R = 1/R_1 + 1/R_2 + 1/R_3 \dots$</p> <p>Total decrease in R in each parallel artery, pressure is same while in series in an Organ Pressure falls</p>	<p>It Depicts how Vol changes with change in Pressure $C = V/P$ (memorize it by CVP)</p> <p>It is the distensibility of vessels. inversely to stiffness and Pressure but directly to Volume. Compliance is higher in Pulmonary circulation than systemic circulation.</p> <p>Veins have → high Capacitance Because highest blood volume is in Veins. (V in formula of Capacitance for Veins and V in Volume)</p> <p>Arteries have → Low Capacitance</p> <p>Aging: decreased Capacitance because arteries become stiffer which increases Pulse pressure</p>

FUNDAMENTAL VASCULAR SYSTEM

Key Components

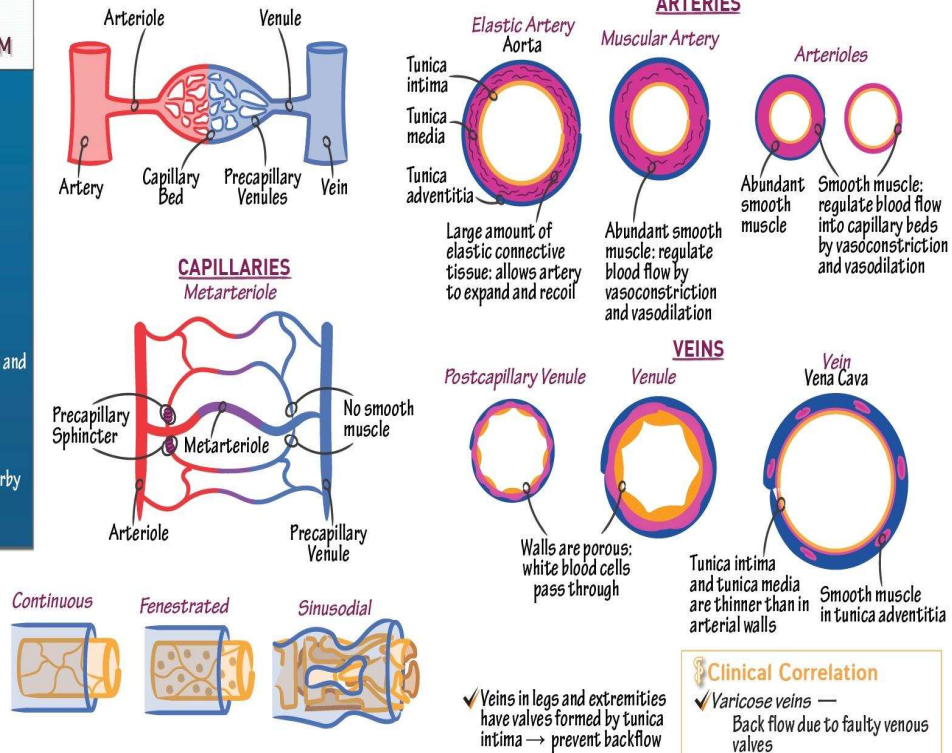
- ✓ Arterial System
 - ✓ Arteries
 - ✓ Arterioles
- ✓ Capillary System
 - ✓ Capillary beds
- ✓ Venous System
 - ✓ Postcapillary venules
 - ✓ Venules
 - ✓ Veins

Vessel Wall Layers

- ✓ Tunica intima: epithelium and connective tissue
- ✓ Tunica media: smooth muscle and elastic connective tissue
- ✓ Tunica adventitia: collagen

Elastic Lamina

- ✓ Supports tunica adventitia
- ✓ Anchors blood vessels to nearby objects
- ✓ Provides stability



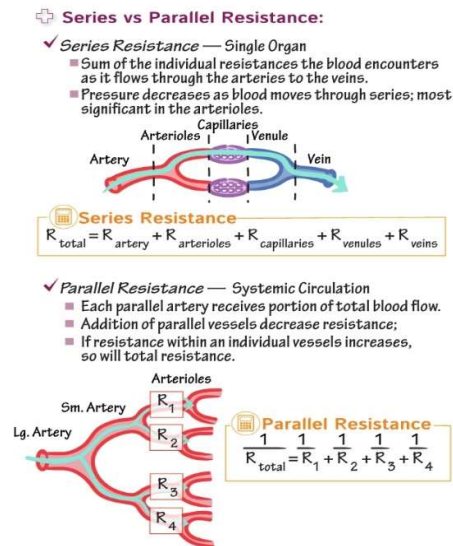
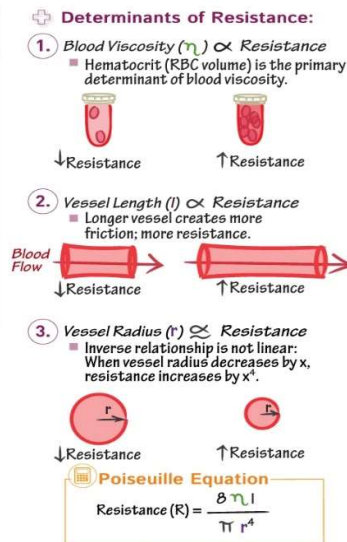
VASCULAR RESISTANCE

Vascular resistance

- ✓ The impediment to blood flow.
- ✓ **Total peripheral resistance** — Resistance to blood flow throughout entire systemic vasculature.
- ✓ **Resistance within an organ** — Eg. resistance within the kidney.

Hyperviscosity syndrome

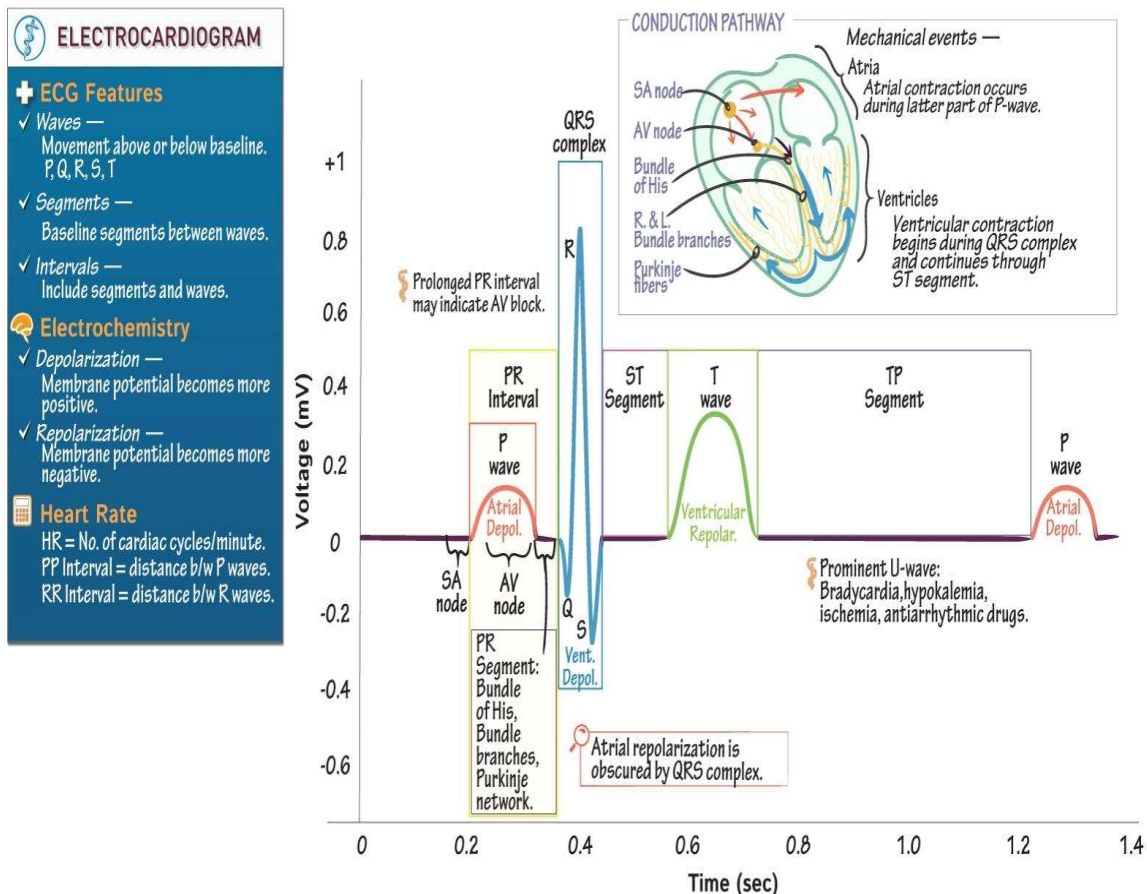
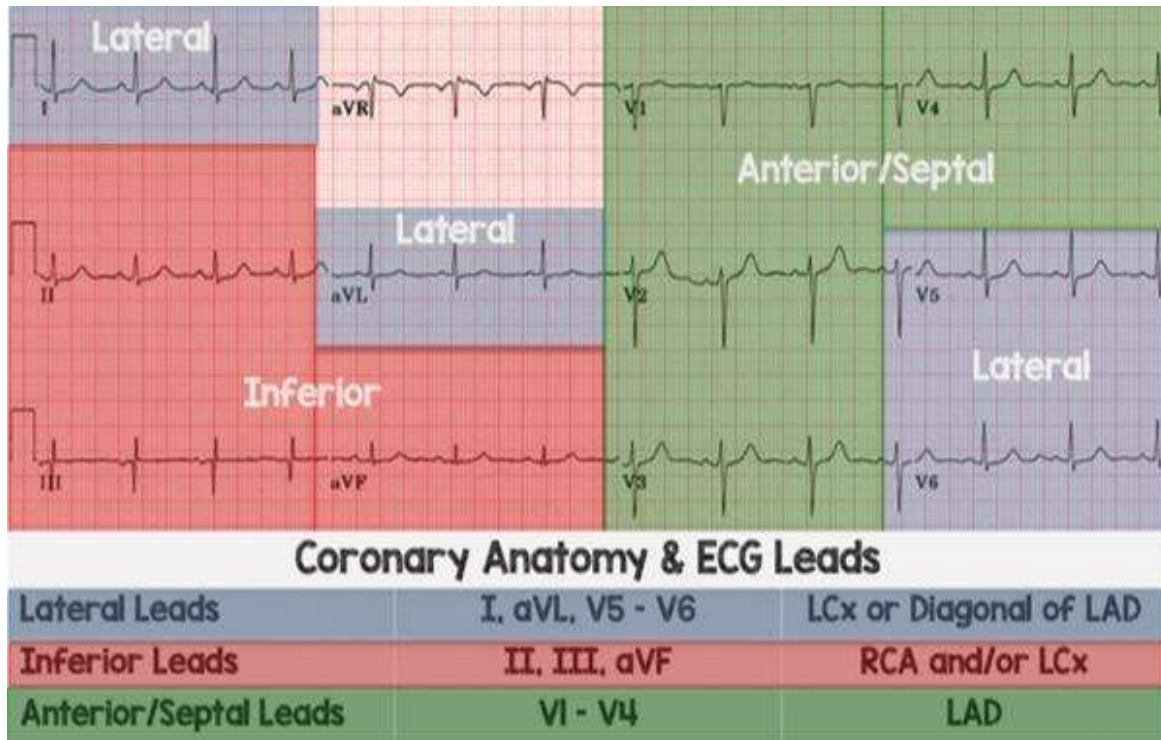
Patients with abnormally elevated levels of blood products often manifest strokes from blood clots as a part of hyperviscosity syndrome.



ELECTROCARDIOGRAM (ECG)

- ECG is a diagnostic tool used to measure and record electrical activity of heart over a period (during cardiac cycle)
- Electrical activity occurs before mechanical activity of the heart.
- ECG represents partially depolarized and partially repolarized state (imp BCQ)
- If this is not in options, then choose Partially Depolarized and Partially Polarized.
- if both above not in options then choose Partially Depolarized state
- ECG consists of Waves, segments and intervals as explained below.
- Wave In an ECG refers to a deflection or a graphical representation of the electrical activity that occurs during specific phases of the cardiac cycle.
- The main waves observed in a standard ECG are P, QRS (Q, R & S) and T wave.
- A segment in an ECG represents a straight line between two waves. These segments have specific names depending on the wave they connect: PR segment and ST segment.
- An interval in an ECG is a combination of waves and segments that are evaluated together to provide important clinical information.
- Common ECG intervals include PR Interval and QT interval.
- 25mm/sec calibration speed is the common one in clinical settings. Vertical lines represent voltage.
- Each small horizontal square or small box = 0.04 sec (40 milli sec)
- Each large square contains 5 small boxes, so large square = 0.20 seconds (200 milli sec)
- Bipolar leads in ECG: Lead I, Lead II, Lead III
- Unipolar Leads: V1, V2, V3, V4, V5, V6 + avR, avL and avF
- It's important to note that the standard 12-lead ECG is the most common type of ECG performed.

ECG Leads Summary		
Standard Limb Leads (Bipolar Limb Leads)	Augmented Limb Leads (Unipolar Limb Leads)	Precordial (Chest) Leads
<p>1. Lead I: It records the electrical activity between the left and right arms.</p> <p>2. Lead II: It records the electrical activity between the left leg and the right arm.</p> <p>3. Lead III: It records the electrical activity between the left leg and the left arm.</p>	<p>1. aVR (Augmented Voltage Right): It records the electrical activity between the right arm and a virtual central point formed by the left arm and left leg.</p> <p>2. aVL (Augmented Voltage Left): It records the electrical activity between the left arm and a virtual central point formed by the right arm and left leg.</p> <p>3. aVF (Augmented Voltage Foot): It records the electrical activity between the left leg and a virtual central point formed by the right arm and left arm.</p>	<p>V1: Fourth intercostal space to the right of the sternum.</p> <p>V2: Fourth intercostal space to the left of the sternum.</p> <p>V3: Midway between V2 and V4</p> <p>V4: Fifth intercostal space in the mid-clavicular line.</p> <p>V5: Anterior axillary line at the same level as V4.</p> <p>V6: Mid-axillary line at the same level as V4 and V5.</p>



<ul style="list-style-type: none"> ○ P wave ○ represents Atrial Depolarization. Atrial repolarization is buried in QRS not evident in normal ECG ○ Atrial repolarization is prominent in Complete heart Block ○ P wave absent in A Fib and Nodal rhythm ○ Q wave represents Initial Vent Depolarization ○ Pathological Q wave in Old MI. ○ R wave shows late vent depolarization ○ Interval b/w R-R is used to find Heart rate on ECG. 	<ul style="list-style-type: none"> ○ PR Interval (0.12 -0.20 sec) ○ From Beginning of P wave to beginning of QRS ○ PR is normally 3 to 5 small squares on ECG ○ PR Represents time needed for impulses to reach from SA node to Ventricle ○ PR Shows Atrial depol to Vent Depolarization. ○ Importance/Significance of PR interval ○ it gives adequate time for Ventricular filling. ○ Sympathetic tone and adrenergic Drugs dec PR interval by ↓ AV nodal delay ○ Parasympathetic drugs or Vagal tone ↑ PR interval by ↑ AV delay.
<ul style="list-style-type: none"> ○ QRS Complex (0.8-0.10 sec) ○ It represents Ventricular Depolarization 	<ul style="list-style-type: none"> ○ ST Segment: ○ Complete Ventricular Depolarization ○ ST segment variations are most imp ECG changes in MI ○ ST represents Plateau phase of ventricular Action potential.
<ul style="list-style-type: none"> ○ QT interval (less than 0.43sec) ○ Represents Entire systolic phase ○ (Vent depolarization + Vent Repolarization) ○ Drugs causing prolonged QT: ○ Fluoroquinolones (Cipro), Macrolides, Azoles, antipsychotics, Anti depressants. ○ Class I+ III anti arrhythmic drugs ○ Electrolytes: HYPOs prolong QT ○ Hypoglycaemia, Hypothermia, HypoK+, HypoMg and HypoCa. ○ Torsade's de Pointes: Long QT syndrome ○ leading cause is Mg deficiency ○ Treatment is IV MgSO4 (also given in eclampsia to dec seizure). 	<ul style="list-style-type: none"> ○ T Wave ○ It represents Ventricular Repolarization ○ T waves changes are earliest in MI. ○ Tall Tented T waves in HYPERKALEMIA(BCQ) ○ Inverted/flat T waves in Hypokalaemia ○ U wave ○ Papillary Repolarization ○ Prominent in Hypokalaemia ○ J waves ○ Seen in Hypothermia.

Conduction from Endocardium to Epicardium is by QT interval While Epicardium to endocardium by QRS

INTERPRETATION OF ECG

Normal ECG: Normal Rate, Regular rhythm and Axis is normal (+60° ideal)

RATE	RHYTHM	AXIS
<ul style="list-style-type: none"> ○ HR is calculated by 2 methods: For Regular rhythm ○ Divide 300 by No. of large squares b/w two consecutive R – R or ○ Divide 1500 by No. of small squares b/w two consecutive R – R waves ○ To Find HR in Irregular rhythms count the number of R waves over a 10 second period and multiply that number by 6. This gives us the average beats per minute (bpm) for a rhythm strip with an irregular heart rate 	<ul style="list-style-type: none"> ○ Lead II, which usually gives a good view of the P wave, is most used to record the rhythm strip. ○ Distance b/w two R-R is measured to see if the rhythm is regular or not. 	<ul style="list-style-type: none"> ○ Normal Axis = b/w -30° and 90°. ○ If axis is more positive than 90 (+90 to 180°). it is referred to as right axis deviation. ○ If the axis is more negative than -30 (-30 to -90) ° it is referred to as left axis deviation.

		<p>Rule of thumb is used to find axis</p> <table border="1"> <thead> <tr> <th></th> <th>Lead I</th> <th>Lead II/aVF</th> <th></th> </tr> </thead> <tbody> <tr> <td>Normal</td> <td></td> <td></td> <td></td> </tr> <tr> <td>(Left Leaving) Left Axis Deviation</td> <td></td> <td></td> <td></td> </tr> <tr> <td>(Right Returning) Right Axis Deviation</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p>Cardiac Axis Thumb Rule</p> <p>Lead I with Lead II /aVF is compared</p>		Lead I	Lead II/aVF		Normal				(Left Leaving) Left Axis Deviation				(Right Returning) Right Axis Deviation			
	Lead I	Lead II/aVF																
Normal																		
(Left Leaving) Left Axis Deviation																		
(Right Returning) Right Axis Deviation																		

. In Sinus Arrhythmia: HR inc During Inspiration & dec during Expiration

SUPRAVENTRICULAR & VENTRICULAR ARRHYTHMIAS

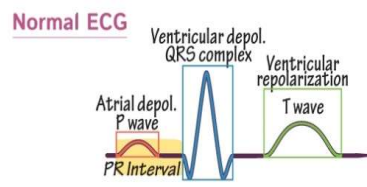
+ Normal Sinus Rate & Rhythm

- ✓ Normal sinus rhythm — SA node sets at 60–100 b/m
P wave precedes every QRS complex
- ✓ Bradycardia — Slow HR (<60)
- ✓ Tachycardia — Fast HR (>100)
- ✓ Sinus arrhythmia — Normal change in HR during respiration.

Cardiac Conduction Pathway

SA NODE — Pacemaker of the heart
AV NODE — Electrical communication between atria and ventricles.

Atria
SA node
AV node
Bundle of His
R & L bundle Branches
Purkinje fibers
Ventricles



Ventricular Arrhythmias
Premature Ventricular Contractions

- ✓ Early ventricular activity (no P wave)
- ✚ Episodic is Normal. 3+ = Tachycardia
- ⊘ Antiarrhythmic drugs can be "proarrhythmic"

- Tachycardia**
- ✓ Consecutive PVCs, broad QRS, 120+ bpm
 - ✚ Can develop fibrillation
 - ⊘ Antiarrhythmics, cardioversion

Torsades de pointes

Spiral
Assoc. w/ Long QT Syndrome
Sudden cardiac DEATH
Rx is Magnesium sulfate

- Ventricular Fibrillation**
-
- ✓ Chaotic
 - ✚ FATAL
 - ⊘ CPR & Defibrillation

Supraventricular Arrhythmias



- ✓ Rapid, regular P waves, Atria = ~300 bpm
- ✚ Coagulation (clots), Low CO, Stroke
- ⊘ Rate & Rhythm restoration, anticoagulants



- ✓ Rapid, irregular/indiscrete P waves
Uncoordinated atrial contraction
- ✚ Coagulation (clots), Low CO, Stroke
- ⊘ See atrial flutter

Premature Atrial Contractions

-
- ✓ Early, deformed P wave
 - ✚ Episodic is normal
 - ⊘ Antiarrhythmic drugs can be "proarrhythmic"

Wolff-Parkinson-White



- ✓ Delta wave, short PR interval, AV node is bypassed
- ✚ Can develop atrial fibrillation
- ⊘ Cardioversion therapy

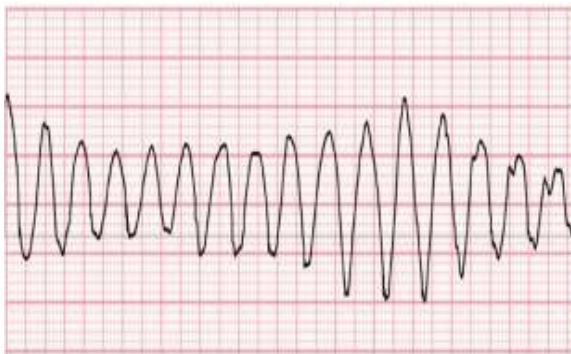
Atrial fibrillation (A Fib)	<ul style="list-style-type: none"> ❖ Irregular R-R interval > P wave Absent ❖ A-fib may happen in Mitral stenosis and thyrotoxicosis → inc risk of Embolic Stroke ❖ DOC for Afib with Heart failure = Digoxin ❖ Rate controlled by Beta blockers (metoprolol) > Ca channel blockers. ❖ Rhythm controlled by Amiodarone -- 1st line for rhythm control. ❖ Without structural heart & without IHD → Flecainide. ❖ Last choice is Cardioversion. ❖ In old age 70+yr: Rate control strategy is preferred over rhythm controls. Metoprolol is used.
Atrial flutter	<ul style="list-style-type: none"> ❖ HR is 200-350/min. ❖ Saw tooth appearance in ECG. ❖ Treated by Catheter Ablation
Supraventricular tachycardia	<ul style="list-style-type: none"> ❖ Narrow complex Tachycardia caused by mostly Av nodal re-entrant tachycardia. ❖ DOC is Adenosine 6mg IV. For diagnosing + terminating SVT. ❖ prophylaxis: by Verapamil
WPW syndrome	<ul style="list-style-type: none"> ❖ Short PR interval. Delta waves + wide QRS. ❖ caused by accessory conduction pathway (bundle of Kent) ❖ WPW syndrome May result in re-entry circuit SVT.
Ventricular fibrillation	<ul style="list-style-type: none"> ❖ Erratic rhythm with no identifiable waves ❖ Fatal without immediate defibrillation and CPR ❖ Cardiac Tissue is most Sensitive to V fib Just at the End of Action Potential (BCQ)
Extrasystole	<ul style="list-style-type: none"> ❖ It causes ↓ Pulse pressure because SV is reduced. ❖ Heart finds less time for filling hence SV is low. ❖ Extra systole is Premature Beat not extra beat. ❖ While Normal contraction after Extra systole causes ↑ PP because contractility is inc, hence SV raised. Heart has adequate time for filling.
Right axis deviation	<ul style="list-style-type: none"> ❖ causes are RBBB, Rt Vent. Hypertrophy But Lt ventricular damage (BCQ)
Left axis deviation	<ul style="list-style-type: none"> ❖ seen in LVH, LBBB, and right ventricular damage. ❖ ECG of HTN patients shows LVH → LAD



(a) NSR



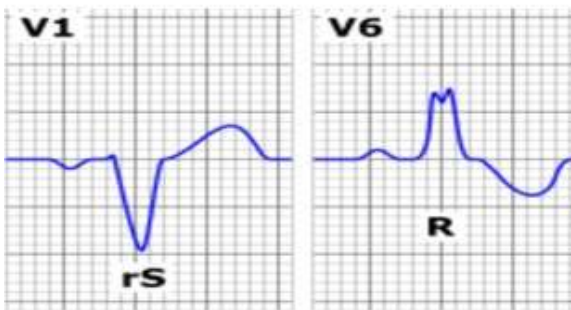
(b) Atrial fibrillation



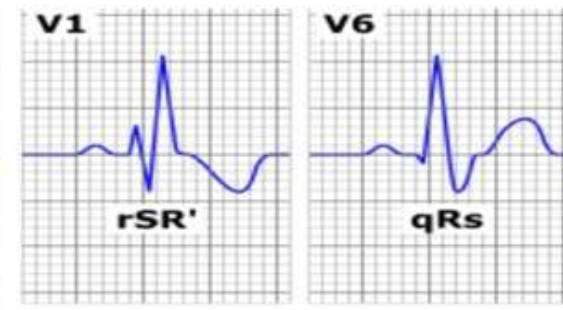
(c) Ventricular fibrillation



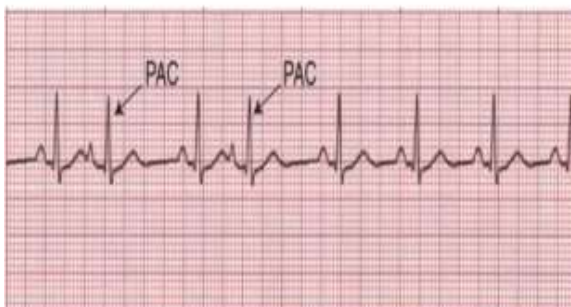
(d) PVC



(e) LBBB



(f) RBBB



(g) PAC



(h) Ventricular tachycardia

CONDUCTION SYSTEM

Conduction Pathway

SA Node → Atria → AV node → bundle of his → R & L bundle branches → Purkinje → Ventricles

- ❖ ventricles directly supplied by Purkinje fibers.(BCQ)
- ❖ All conduction system is supplied by Right Coronary Artery except Right bundle branch which is by LCA
- ❖ LBB supplied by both RCA&LCA. Bundle of HIS supplied by RCA
- ❖ Apex of Heart by Left anterior descending artery > Rt Marginal.

Location Of Conducting Pathway/System

- ❖ SA node= Sub Epicardium (Upper portion of Crista terminalis) (BCQ) -- Supplied by RCA 60%.
 - Parasympathetic effect inc K⁺ permeability of SA node (BCQ)
- ❖ AV node: ENDOCARDIUM (poster inferior part of interatrial septum. RCA supplies it.
- ❖ Conducting System: Bundle of His and bundle branches → Sub- Endocardium (BCQ)
- ❖ Conducting system of Heart is a specialized cardiac tissue (BCQ)

Speed of Heart Rate	Speed of Conduction
<ul style="list-style-type: none"> ○ SA node: 60-80 bpm ○ AV: 40-60 bpm ○ Purkinje: 20-40 bpm ○ SA node > AV > Purkinje 	<ul style="list-style-type: none"> ❖ PURKINJI have highest Conduction velocity due to: ❖ Wide Diameter > inc Gap junctions + inc Na channels > less Myofibrils and short refractory period. ❖ Purkinji > Bundle of HIS > Atria > ventricles > SA > AV ❖ Slowest conduction is of AV Node. ❖ Don't confuse speed of Heart rate with conduction speed/ Velocity.
Key facts	
<ul style="list-style-type: none"> ○ SA node has Slowest but Dominant Pre- Potential due to action Potential by Ca²⁺ channels. ○ SA node is pacemaker of Heart because it generates impulse at Faster Rate > Automaticity ○ Heart behaves as Syncytium due to Gap junctions ○ Intercalated disc maintain cell to cell cohesion. ○ Sarcomere runs from Z - Z lines and is the contractile unit of cardiac muscles same as Skeletal Muscles. ○ Sarcomere contains thick (myosin)& thin (actin, tropomyosin and troponin) ○ Sarcomere seen on H zone: what will be seen on Relaxed muscle → Thick filament ○ Thick filaments comprise mainly Myosin & some part of Actin ○ Cardiac Myocytes are striated, have single Nuclei. Both Alpha + Beta Myosin Present. ○ <u>During contraction:</u> ○ A band is Unchanged. H zone disappears ○ Sarcomere + I band shorten (BCQ) 	

ACTION POTENTIAL

- Inward current depolarizes while outward causes Repolarization.
- Atria + Vent + Purkinji: 5 phases
- SA node: 3 phases → ph1 and 2 absent
- Action potential of A,P,V/Cardiac muscle + Pacemaker activity of SA node is due to Na⁺ channels
- Remember, APV vehicle moves fast so for fast conduction Na⁺ used.
- Action potential of Pacemaker (NOT pacemaker Activity) is due to Ca²⁺ channels
- But pacemaker activity is by Na⁺ channels. Both are different so Don't confuse them.

Phases of AP of Atria, Ventricles and Purkinje	Phases of AP of SA Node
<p>phases</p> <ul style="list-style-type: none"> Ph0: Upstroke by inward Na^+ current Ph1: initial Repol by K^+ efflux Ph2: Plateau phase → Due to Ca^{2+} influx and K^+ efflux. ST segment represents Plateau phase. Ph 3: Repol. due to K^+ efflux mainly Ph 4: is RMP -both outward and inward K^+ current equal <p>Summary</p> <ul style="list-style-type: none"> Ph0 : Na^+ influx Ph2: Ca^{2+} influx mainly Ph 1,2,3,4 : involve K^+ efflux. 	<p>Three Phases Only</p> <ul style="list-style-type: none"> Ph 0: Upstroke by Ca^{2+} influx. Ph3: Repolarization by K^+ efflux Ph4: for Pacemaker activity → Slow Depolarization -- Uses Funny Sodium channels (BCQ)

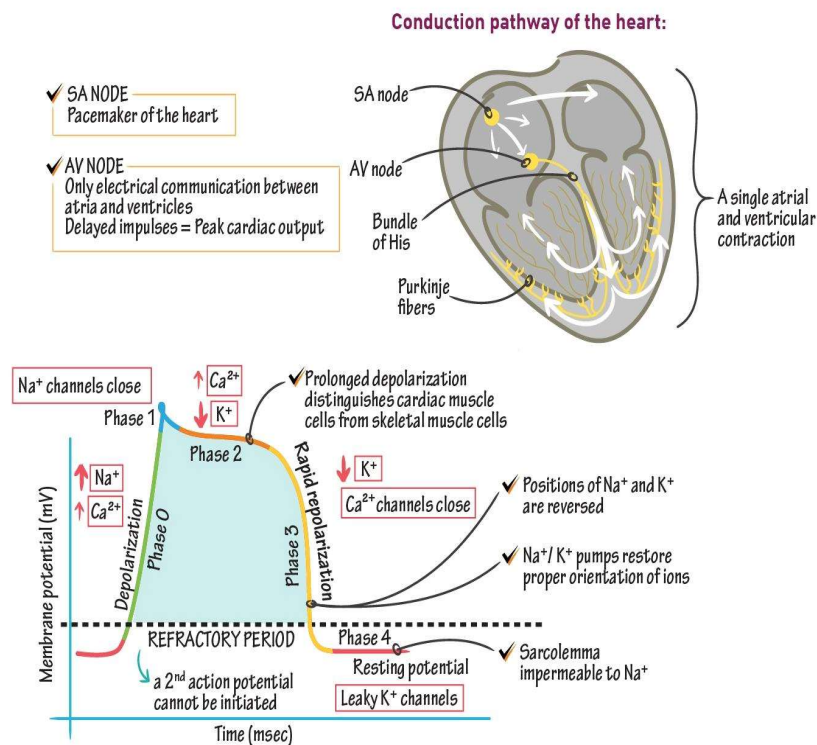
FUNDAMENTAL CARDIAC CONDUCTION

Cardiac Muscle Cells

- ✓ Contractile (99%)
- ✓ Autorhythmic (1%)
 - ✓ initiate action potentials

Specialized Areas with Autorhythmic Cells

- ✓ Sinoatrial node (SA node)
- ✓ Atrioventricular node (AV node)
- ✓ Bundle of His
- ✓ Purkinje fibers



Two phases of Refractory Period

- **Absolute refractory period:** No stimulus of any Strength will trigger AP. Lasts as long as Na gates Are open, then inactivated.
- **Relative refractory period:** Only especially strong Stimulus will trigger new AP. K⁺ gates are still open and Any effect of incoming Na is Opposed by the outgoing K⁺. Generally, lasts until Hyperpolarization ends
- Only a small patch of neuron's Membrane is refractory at one Time (other parts of the cell can Be stimulated)

HEART BLOCKS		
First degree heart block	Second degree heart block	Third degree heart block
<ul style="list-style-type: none"> ❖ PR interval is Prolonged Due to block at AV node ❖ Treatment is NOT needed. ❖ P and QRS Normal in ratio 1 : 1 	<ul style="list-style-type: none"> ❖ Mobitz1(Wenckebach): Progressive inc in PR interval due to AV nodal block until a beat drops. ❖ Regularly irregularly Rhythm ❖ Mobitz-2: Dropped Beat without progressive lengthening of PR interval Rhythm is Regular. ❖ Abnormality in HIS – Purkinje system ❖ P: QRS ratio changed 2 :1 or 3: 1 	<ul style="list-style-type: none"> ❖ Complete heart block or 3rd degree block. ❖ P wave has no relation with QRS. ❖ Atria and Ventricles beat independently because NO conduction by AV node. ❖ Giant > Cannon “a” wave on JVP ❖ Treated by Pacemaker.
Key Facts <ul style="list-style-type: none"> ➤ Pacemaker is placed in Rt Ventricle (moderator Band) ➤ Pacemaker is required for defect in SA node. ➤ Pacemaker required for defect in CONDUCTION of AV Node. ➤ NOTE: Observe the Diff of Word Conduction in above 2 Points 		

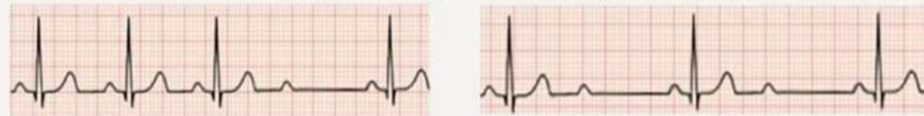
- If the R is far from the P, then you have a 1st Degree



- PR gets longer, longer, longer, drop, it's a case of Wenckebach!



- If some R's don't get through, prepare to pace that Mobitz II!



- If the R's & P's don't agree, prepare to PACE that 3rd degree!



Terms Related to HR and Conduction Velocity		
Inotropy	Chronotropy	Dromotropy
<ul style="list-style-type: none"> ○ It refers to Force of contraction. ○ Dependent on Ca²⁺ ○ determined by sarcomere length. ○ Digoxin inc FOC by inc Ca²⁺ inside cell 	<ul style="list-style-type: none"> ○ It Refers to Heart Rate ○ by changing in firing rate at SA Node 	<ul style="list-style-type: none"> ○ It refers to conduction velocity. ○ by changes at AV Node velocity ○ +ve Inotropic, Chrono, dromotropic means inc in these variables. ○ negative means Dec. in these factors.
Effect of Autonomic Nervous system		
<p>Sympathetic system: B1 receptors on heart. (BCQ) 1 heart so B1 → +ve chronotropic + Dromotropic</p> <p>Parasympathetic system: M2 receptors on Heart → -ve chronotropic and -ve dromotropic</p> <p>-ve dromotropy occurs by Dec Ca in AV node so PR prolongs</p> <p>-ve chronotropy: Phase4. Sodium current . reduction by Funny Na channels</p> <p>Ventricular muscles don't have. Autonomic innervation so these changes are due to SA node and AV nodes.</p>		
Sympathetic system main effect is on Heart and Vessels while Parasympathetic effect mainly on GIT + Glands		

HEART SOUNDS			
First Heart Sound (S1)	Second Heart Sound (S2)	Third Heart Sound (S3)	Fourth Heart Sound (S4)
<p>Closure of Mitral and Tricuspid valves.</p> <p>S1 indicates isovolumetric contraction.</p> <p>S1 is of longer duration than S2</p>	<p>Closure of Semilunar valves i.e. Aortic + Pulmonary Valves</p> <p>S2 → Isovolumetric Relaxation.</p> <p>S2 has More Frequency + Pitch than S1.</p>	<p>Ventricular gallop or Gallop rhythm</p> <p>Dilated Ventricles with Rapid Filling/inflow</p> <p>Normal in Child, athletes, or Pregnancy</p> <p>Associated with Valvular disorders, MR, and Heart failure in adults.</p>	<p>Atrial gallop or atrial kick due to Stiffened and Hypertrophic ventricles e.g., Hypertrophic Obstructive cardiomyopathy.</p>
Imp Concepts			
<ul style="list-style-type: none"> ○ Isovolumetric Contraction: S1 and for Isovolumetric relaxation: S2 ○ Rapid Filling. Inflow/Dilated Ventricles: S3 ○ Stiff/Hypertrophic Ventricles + atrial systole: S4 ○ Tachycardia shortens PR interval so S1 will be at Lower limit/range of PR (BCQ) ○ When all Valves are closed Ventricular vol is constant so called Isovolumetric. ○ Normal physiological splitting of S2(in inspiration) is due to delayed closure of pulmonary valve > Early closure of aortic valve. Fixed splitting of S2 seen in ASD (No effect of inspiration). Wide splitting is inspiration due to early closure of pulmonary valve, seen in: Pulmonary HTN, pulmonary Stenosis and RBBB. ○ Reverse splitting of S2 is heard on expiration and due to delayed aortic valve closure e.g Systemic HTN, LBBB, Aortic stenosis. 			

Summary of S2 Splitting

- Normal & wide splitting on inspiration whereas Reverse splitting on expiration. both caused by Delayed Closure of Pulmonary > Early aortic closure.
- **ASD: Fixed splitting**, no role of Respiration
- Right sided diseases affect Wide splitting & left sided diseases affect Reverse Splitting

CARDIAC CYCLE (0.825 seconds)

1. **Atrial systole:** Preceded by P wave on ECG and a wave in JVP. Gives S4 in vent hypertrophy.
2. **Isovol. Contraction(S1):** Period of max O₂ consumption. B/w Mitral closure and Aortic valve opening. Pressure is raised but No blood leaves ventricles as Aortic valve is still closed. Begins during QRS.
3. **Rapid Vent. Ejection:** most of SV is ejected during it as Ventricle pressure becomes more than Aortic pressure thus causing opening of Aortic Valve and atrial filling just begins
4. **Reduced/Slow Vent Ejection:** Atrial filling continues and pressure in both Vent & Aorta falls due to blood flowing off from vent and aorta to arteries.
5. **Isovol. Relaxation(S2):** aortic valve closes followed by pulmonary valve closure
Inspiration delays closure of Pulmonary valve leading to S2 splitting
Vent vol is constant because all valves are closed but pressure falls rapidly as Vent are relaxed now.
6. **Rapid Vent filling(S3):** Mitral valve opens when vent pressure gets less than atrial pressure. Vent filling begins.
7. **Reduced Filling/Slow Vent Filling:** Longest phase -- Effected by HR.
Tachycardia decreases this slow Vent filling phase. (BCQ)

MAIN CONCEPT

- 2 phases of Ejection & Filling preceded by Isovol contraction and Relaxation respectively.
- Atrial systole causes S4 in hypertrophied Ventricles by Vent filling. So now blood is in Ventricles.
- isovol contraction causes increased Pressure only but No blood ejects from ventricles as valves are closed.
- Now inc Pressure in Ventricles causes opening of Aortic + Pulmonary valves. When valves are opened, blood rushes/ejects from Vent to aorta and aorta to large arteries.
- Ejection is of 2 types Rapid and Reduced as explained above.
- When Blood ejected Vent are relaxed now. so that is Isovol. Relaxation (S2)
- But During Ejection Atrial filling continues which further causes Vent filling .
- Vent filling is of 2 types Rapid and Reduced same as Ejection.
- Rapid Vent filling produces S3 and Red /slow filling which is dependant of HR

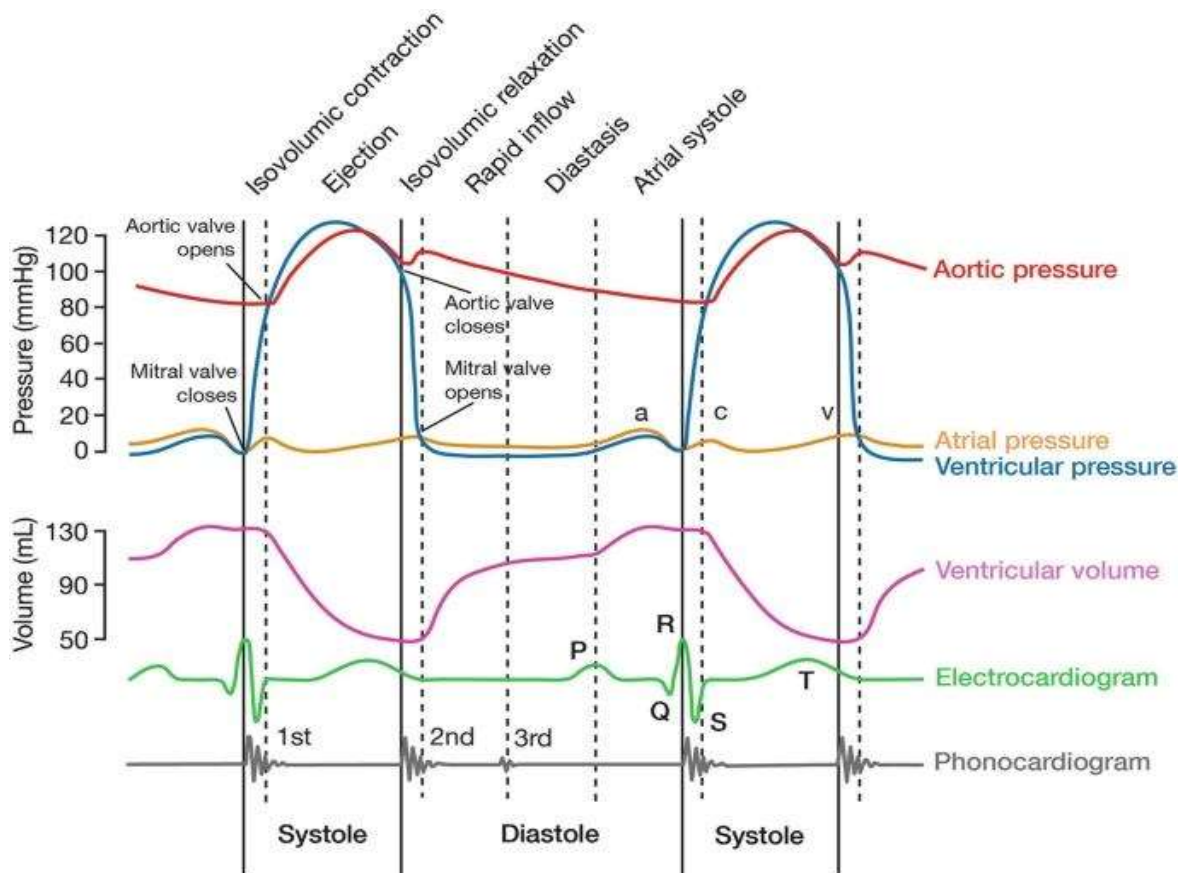
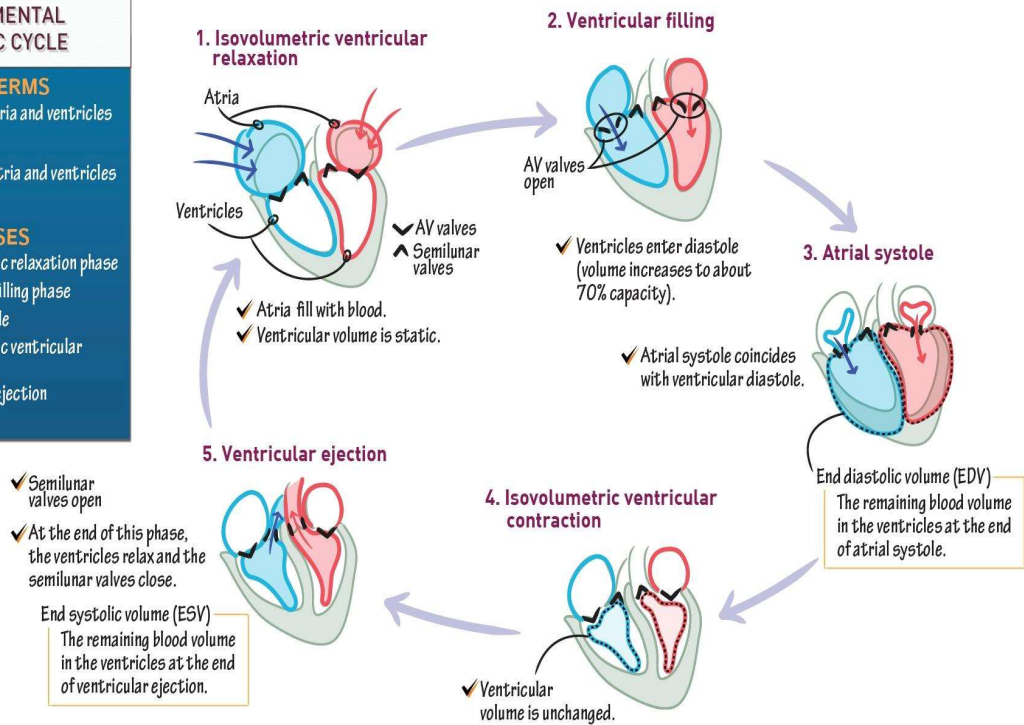
FUNDAMENTAL CARDIAC CYCLE

KEY TERMS

- ✓ **Systole:** the atria and ventricles contract.
- ✓ **Diastole:** the atria and ventricles relax.

PHASES

- ✓ 1. Isovolumetric relaxation phase
- ✓ 2. Ventricular filling phase
- ✓ 3. Atrial systole
- ✓ 4. Isovolumetric ventricular contraction
- ✓ 5. Ventricular ejection



CARDIAC PRESSURES

- Rt Vent Pressure at which Pulmonary valve opens is= 8mmHg
- Rt Vent Pressure in diastole: 0-8mmHg and in systole: 25mmHg
- Lt Vent P at which aortic valve opens is 80 mmHg.
- Max Vent Pressure : Rapid Ejection
- Max aortic Pressure: Reduced Ejection
- Min Vent Pressure : Rapid Filling
- Min Aortic Pressure: Isovolumetric contraction
- Max Vent FILLING: Rapid Filling (S3)
- Max Vent FILLED: Atrial systole (S4)
- **Tip to Memorize above Pressures**
- At Max Pressure Ejection occurs as Ejection requires force and Pressure
- At Min Pressure Filling occurs.
- The Word Rapid used with Ventricle and Reduced used with Aortic pressure

JUGULAR VENOUS PULSE (JVP)

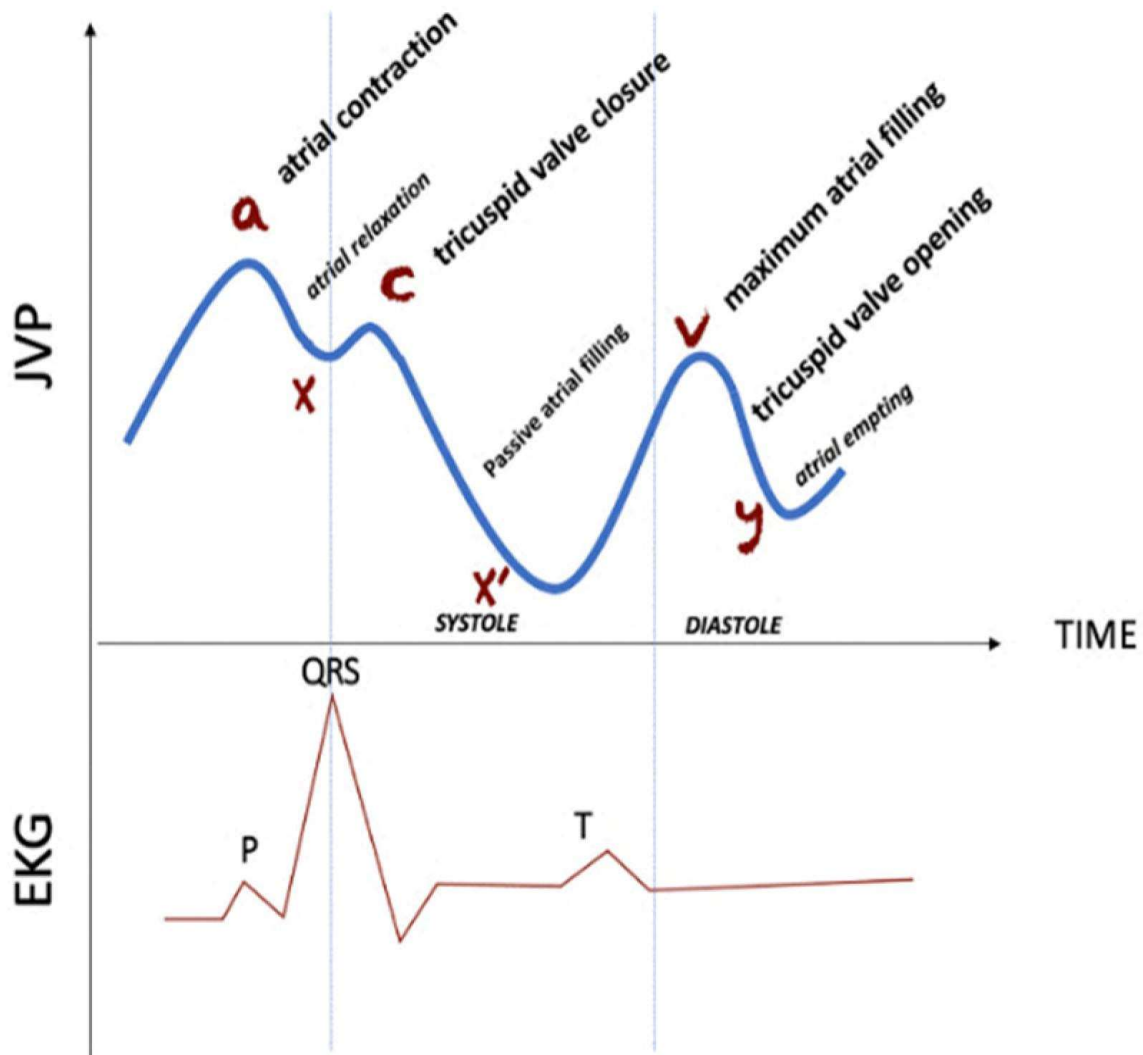
- 📌 Normal JVP is 6-8cm above mid point of Rt Atrium
- 📌 It is an indirect measure of CVP which measures Rt Atrial Pressure.
- 📌 Present b/w 2 heads of SCM muscle
- 📌 Not palpable+ Occludable
- 📌 Falls with Inspiration and Sitting erect

JVP Waveform

- 📌 Ascents+ 2 Descents
- 📌 A wave: Atrial contraction (A for Atria). a wave coincides with PR SEGMENT, Not Interval.
- 📌 C wave: Rt vent Contraction (CV)
- 📌 X Descent: During Rapid Vent ejection
- 📌 V wave: Closed Tricuspid Valve downward displacement. Filling against closed tricuspid Causes inc Rt Atrial pressure. Mnemonics: (Villing/filling)
- 📌 V wave → isovolumetric Relaxation(BCQ)
- 📌 Y Descent: RA emptying into RV (Y in emptying)

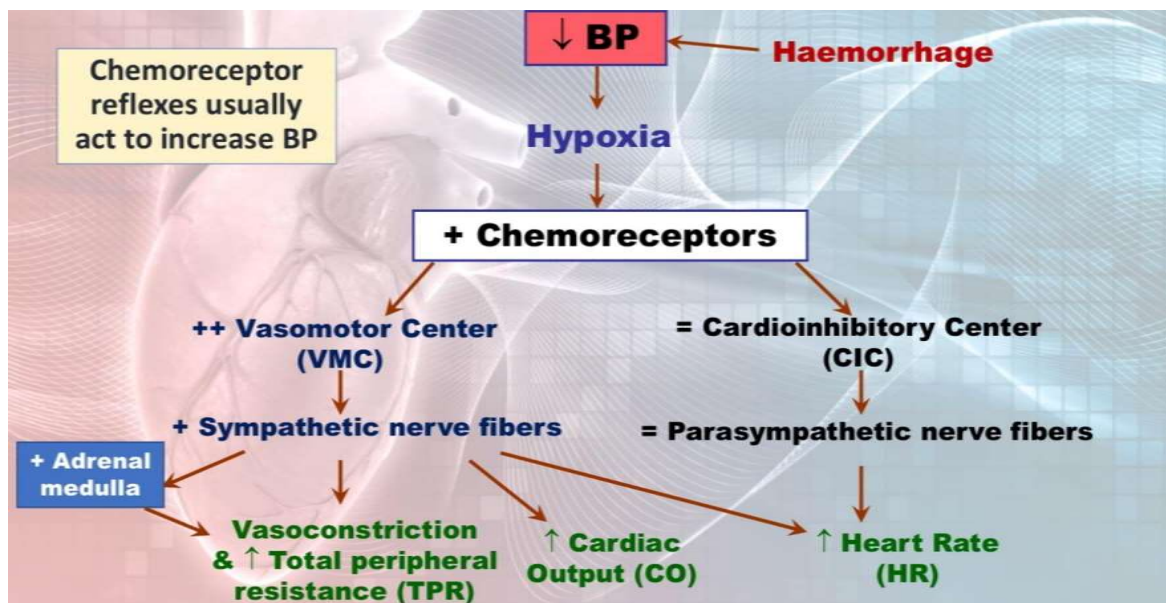
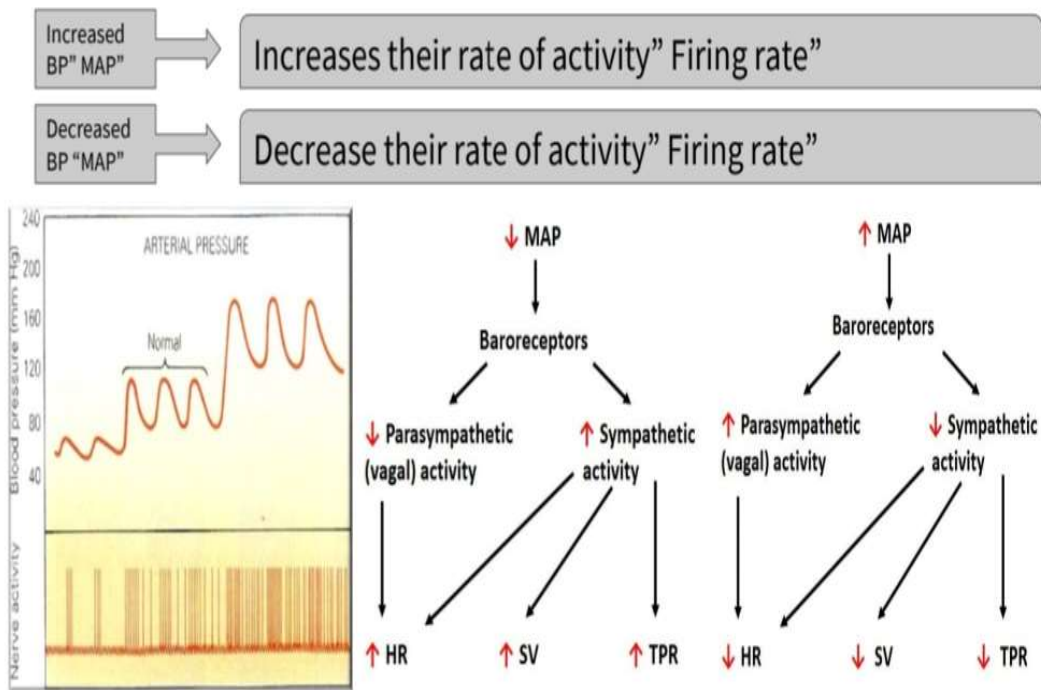
a wave	<ul style="list-style-type: none"> ➤ Canon a wave in A fib ➤ Giant a wave in Complete Heart block ➤ Prominent a in tricuspid stenosis Pulmonary stenosis+ Pulmonary HTN Because in stenosis Pressure is raised so a wave will be prominent
v wave	<ul style="list-style-type: none"> ➤ V Wave Prominent in Tricuspid Regurge ➤ V wave is filling wave. anything inc Filling will make V prominent/more Raised. ➤ e.g. Tricuspid regurge inc Filling due to backflow and incompetent valve hence will make Prominent V wave
x descent	<ul style="list-style-type: none"> ➤ X Descent Absent in RHF and T.R ➤ As X is by Tricuspid downward displacement. ➤ So, diseases of Rt heart and Tricuspid Valve will affect it
y descent	<ul style="list-style-type: none"> ➤ Slow y descent in Tricuspid stenosis as y descent is formed by emptying ➤ In stenosis, emptying is slow. Hence slow Y descent. ➤ Y descent Rapid in Constrictive Pericarditis as Constrictive force around heart will increase emptying so rapid descent

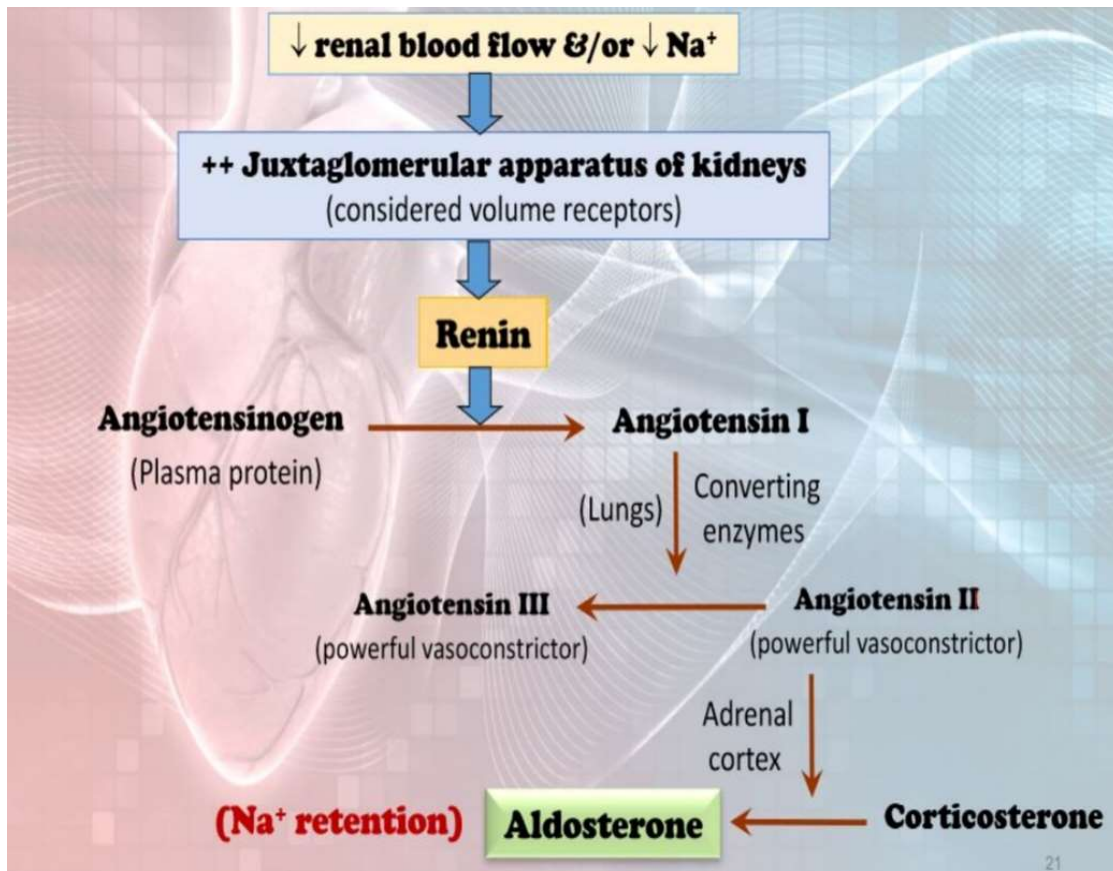
- Absent Y descent in Cardiac Tamponade as the Pressure of fluid around heart doesn't let it Empty so absent Y descent



REGULATION OF ARTERIAL PRESSURE (BLOOD PRESSURE)	
Short term	<ol style="list-style-type: none"> 1. Baroreceptors reflex mechanism – shortest, fastest, immediate response in shock. 2. Chemoreceptors reflex (explained in the flowchart given below) 3. CNS ischemic response – most potent for BP regulation when MAP is below 60. <p>Baroreceptor Mechanism</p> <ul style="list-style-type: none"> ○ They are the stretch receptors located at the vasa vasorum of vessels. ○ Acute Hemorrhage → dec Arterial pressure due to low blood vol. ○ Dec Stretch on Carotid Sinus receptors and ↓ Carotid sinus nerve activity leads to ↑ Sympathetic activation. ○ SANS activation → Inc HR+ contractility + vasoconstriction. Vasoconstriction → inc TPR → inc Venous return → inc MSFP ○ Mean systemic Pressure inc. So, they all bring back Pa (arterial pressure) to Normal. <p>Simple Trick for Baroreceptor Mech:</p> <ul style="list-style-type: none"> ○ If B.p Drops → dec firing & dec carotid sinus nerve activity → inc HR. ○ Hence Firing rate directly to B.P & inversely to Heart Rate (remember the mechanism above)
Intermediate	<ol style="list-style-type: none"> 1. Stress relaxation of vasculature 2. Renin – AT vasoconstrictor mech 3. Capillary fluid shift mechanism
Long-term	<ol style="list-style-type: none"> 1. Renin – AT aldosterone mechanism – most effective and important response overall. 2. Renal body fluid mechanism <ul style="list-style-type: none"> ○ Hemorrhage decreases Renal blood flow → Renin released from JG cells causes Angiotensinogen conversion → AT1. ○ AT1 conversion → AT2 occurs in Lungs <p>Angiotensin - II Functions:</p> <ul style="list-style-type: none"> ○ It is a Vasoconstrictor which inc TPR + arterial pressure ○ Inc Synthesis of Aldosterone. Aldosterone → Na⁺ absorption leads to raised ECF + blood vol. ○ Inc ADH release → inc Water Retention which further raises Blood Vol. ○ Keep in mind that ADH is more powerful vasoconstrictor than AT – II
Summary	<ul style="list-style-type: none"> ○ Renin-AT2 system(Long Term and Major mechanism) ○ Short Term + Fastest, earliest, and immediate response in shock) – baroreceptor reflex ○ Baroreceptors Respond Maximally to Rapidly Increasing BP, NOT Dec B.P ○ (Because they are stretch receptors so respond to inc Stretch by increased B.P) ○ Baroreceptors respond to Decreasing Arterial Pressure (Pa) (Learn the diff in above 2 statements) ○ Most rapid response to decreased B.P is Baroreceptors ○ CNS ischemic response – most potent, activated when MAP below 60. ○ Aortic bodies innervated by CN IX ○ Carotid bodies at the bifurcation of CCA - innervated by CN X. ○ most imp for B.p maintenance during or within Shock is Baroreceptor system. ○ Overall, most imp for Arterial Pressure& B.p maintenance is Renin-AT2 system.

Firing Rate of Baroreceptors





Special Circulations

- Autoregulation: blood flow remains constant over wide range of Pressures.
- Autoregulation seen in; Heart + brain + Kidneys+ Lungs
- Autoregulation NOT seen in Liver > Skin
- Cerebral + Coronary circulation exhibit Hyperaemia & entirely controlled by Local Metabolites
- Most important for Cerebral circulation is CO₂.
- CO₂ causes Vasodilation in brain circulation
- Most imp for Coronary is Hypoxia(Low O₂) & adenosine
- Blood flow control of Skeletal Muscles At rest by Sympathetic System. During exercise by Local Metabolites.
- Skin Entirely controlled by Sympathetic system
- In strenuous exercise Blood flow to skin is reduced
- **In Exercise:**
- Blood flow Unchanged in: Brain.
- Blood flow Decreases in RENAL > Splanchnic circulation
- **Remember:**
- Liver receives 27 % of CO
- Kidney receives: 22% of CO. (BCQ)
- Max blood flow per minute is in Liver
- Least blood flow per minute in Heart

- Max blood flow per 100 gram of tissue : Carotid bodies > Kidney (BCQ)
- Which organ has Max O₂ consumption: Liver
- Max O₂ consumption per 100 gram of tissue: Heart (BCQ)
- Least O₂ Consumption: Skin
- Max O₂ extraction from the blood Heart (BCQ)

Controversial BCQs

- Obese man wears tight collar feels dizziness due to = increased VENOUS Compliance.
- **Reason** : Tight collar raises pressure in carotid sinus, so Parasympathetic activation leads to Vasodilation
→ Inc compliance. Low blood supply to brain causes Syncope due to Vasodilation, bradycardia & low B.P

From Sitting to Standing:

- Decreased parameters: HR, B.P, VR, Contractility, SV, EF
- As a Compensatory response due to dec HR and Blood Pressure → Inc firing of baroreceptors leads all these factors back to normal so, **↑** HR + VR + Contractility +SV + EF. all factors **↑**
- if Q is about ; from sitting to standing Compensation occurs by which Mechanism ?
 - Then it will be **↓** Venous Return
- If Q is regarding that from sitting to standing which is compensatory response
 - Then **↑**: HR, VR, SV, EF, and contractility. All these **↑**
- Learn the diff b/w these 2**
- Compensatory Mechanism → decreased VR
- But Response/Compensatory response is **↑**HR, VR, SV, EF.

PAST PAPER BCQS – ONE LINERS

1. Total Peripheral Resistance (OR) Systemic vascular Resistance: Vasoconstriction by Sympathetic ↑ TPR. Vice versa for Parasympathetic.
2. Index of TPR: Diastolic BP
3. If Rt Atrial Pressure= then HR increases
4. Max pressure in aorta in = Slow Ejection phase Or Reduced ejection.
5. Pulse Wave velocity detects blood flow to extremities
6. Deep inspiration leads to = inc pulmonary compliance > dec VR
7. S4: Ventricular filling during Atrial systole
8. S3: Vibration of Ventricle during Rapid Vent inflow/Rapid Filling.
9. lowest aortic pressure in = Isovol contr.
10. Measurement of CO by Thermodilution may be inaccurate due to inspiratory changes in Pulmonary artery temperature.
11. a wave of JVP corresponds to PR SEGMENT
12. ↑ CVP due to ↓ HR
13. Dec in HR Affects SYSTOLIC B.p more (dec)
14. Inc in HR affects diastolic B.p more .it ↓
15. Ventricular systole = QT/RT interval
16. vent Plateau = ST Segment.
17. Regarding Coronary arteries = 2 Coronary + Auricular + 1AV nodal + 1septal.

18. Heart behaves as Syncytium due to Gap junctions
19. Intercalated disc maintain cell to cell cohesion.
20. Sarcomere runs from Z - Z lines and is the contractile unit of cardiac muscles same as Skeletal Muscles.
21. Sarcomere contains thick (myosin)& thin (actin, tropomyosin and troponin)
22. Sarcomere seen on H zone: what will be seen on Relaxed muscle → Thick filament
23. Thick filaments comprise mainly Myosin & some part of Actin
24. Kidney receives: 22% of CO
25. Max blood flow per minute is in Liver
26. Least blood flow per minute in Heart
27. Max blood flow per 100 gram of tissue : Carotid bodies > Kidney
28. Which organ has Max O ₂ consumption: Liver
29. Max O ₂ consumption per 100 gram of tissue: Heart
30. Least O ₂ Consumption: Skin
31. Max O ₂ extraction from the blood Heart
32. Most important for Cerebral circulation is CO ₂ .
33. CO ₂ causes Vasodilation in brain circulation
34. 60 to 70%energy provided by FATS (BCQ) and Rest by Glucose & Lactate.
35. V wave: isovolumetric contraction
36. CO is Unchanged in Sleep.
37. While CO inc in Exercise (highest 700%inc) > Anxiety/excitement > Eating and pregnancy
38. 60 to 70%energy provided by FATS (BCQ) and Rest by Glucose & Lactate.
39. CO is Unchanged in Sleep.
40. Autoregulation NOT seen in Liver > Skin
41. Rt Vent Pressure in diastole: 0-8mmHg and In systole: 25mmHg
42. Lt Vent P at which aortic valve opens is 80 mmHg
43. Max Vent Pressure : Rapid Ejection
44. Max aortic Pressure: Reduced Ejection
45. Min Vent Pressure : Rapid Filling
46. Min Aortic Pressure: Isovolumetric relaxation
47. Baroreceptors Respond Maximally to Rapidly Increasing BP, NOT Dec B.P
48. Pacemaker is placed in Rt Ventricle (moderator Band)
49. Pacemaker is required for defect in SA node
50. Pacemaker required for defect in CONDUCTION of AV Node.
51. Pathological Q wave in Old MI.
52. VR is inc by Skeletal Muscle contraction (Pump)in Legs as in Exercise. Soleus muscle of leg is known as 2nd Heart.
53. Athletes have high Resting CO & inc Stroke vol but Dec Heart rate(imp BCQ)
54. O ₂ consumption is 250 ml/min
55. O ₂ consumption inc by inc Heart size , contractility ,heart rate and afterload.
56. Sympathetic system: B ₁ receptors on heart. (BCQ) 1 heart so B ₁ → +ve chronotropic + Dromotropic
57. Parasympthetic system:M ₂ receptors on Heart → -ve chronotropic and -ve dromotropic

DISEASES OF THE VESSELS & HEART**ATHEROSCLEROSIS**

- Disease of Tunica intima of elastic arteries + large and medium sized muscular arteries.
- Atherosclerosis is the 90% cause of IHD. It damages elastic fibers of vessel also.

Risk Factors	<ul style="list-style-type: none"> • Modifiable: Smoking, HTN, DM & Hyperlipidaemia • Non-Modifiable: Age, Male, Family history & post-menopausal status due to (↓ oestrogens, dec Cholesterol) • Lipoprotein a is a form of LDL containing Apo B100. It inc risk of IHD. • Type A personality also inc the Risk.
Pathogenesis	<p>Chronic Endothelial injury in Obese/Smoker/Diabetic/Hypertensive/Hyperlipidaemic individual (male more common) leads to Deposition of fibro fatty plaque in INTIMA of vessels.</p> <p>Composition Of Plaque Consisting of 3 components</p> <ol style="list-style-type: none"> Lipids (LDL main) Cells: Macrophages : Foam cells and T Cells & Smooth Muscle cells) Extracellular matrix (ECM) includes Collagen + elastin. <ul style="list-style-type: none"> ▪ FIBROUS CAP is Pathognomonic ▪ Fatty Streak are earliest lesions < 1mm. Composed of Foam cells (Lipid Laden macrophages)
Vessels Involved	<p>In Descending Order</p> <ol style="list-style-type: none"> Abdominal Aorta (infra renal) most common site overall (L1 – L3) Coronary Popliteal Des Aorta Int carotid circle of Willis
Complications	<p>Calcifications, Aneurysm, Ulceration, Thrombus and Embolism Most lethal complication is Thrombus.</p> <p>Common cause of Pale infarct in Organs : Thrombus > Atheroma -While Red infarcts are Embolic.</p> <p>Leireche Syndrome : Occlusion of Aorta at Common Iliac vessels commonly. Occlusion may also occur at femro-popliteal junction. Leads to Buttock claudication + sexual impotency with weak femoral pulse</p>




ARTERIOSCLEROSIS

(Hardening of small arteries and arterioles)

Types	<ul style="list-style-type: none"> • Hyaline Arteriosclerosis: feature of DM & chronic Hypertension. Due to fibrin and plasma protein Leakage from vessels.
	<ul style="list-style-type: none"> • Hyperplastic Arteriosclerosis: feature of Malignant severe HTN Laminated, Concentric. Onion skin appearance (BCQ) → Fibrinoid necrosis/necrotizing arteriolitis is seen. Kidneys appear Flea-bitten in severe HTN with multiple punctate haemorrhages

Monckeberg Medial Sclerosis Or Medial Calcific Sclerosis

- Dystrophic calcification of mostly Ulnar and Radial arteries in older than 50+age
- Pipe stem appearance on X ray and Ring Like calcifications in tunica Media of vessels

<p>ANEURYSM</p>	<ul style="list-style-type: none"> Localised dilatation of vessel or part of heart. Atherosclerosis > HTN are main causes. Also includes the factors causing Atherosclerosis Radio-Radial delay seen in Aortic Aneurysm/ dissection and coarctation of aorta. <p><u>TYPES</u></p> <table border="1"> <tr> <td data-bbox="456 369 654 558"> <p>True aneurysm</p> </td><td data-bbox="654 369 1403 558"> <p>Involving all 3 layers of vessel/Heart e.g in syphilis, atherosclerosis, and Lt Ventricle aneurysm True aneurysm has 2 types :</p> <ol style="list-style-type: none"> Saccular (spherical outpouching) Fusiform (Circumferential) – Most common type. </td></tr> <tr> <td data-bbox="456 558 654 667"> <p>False Aneurysm</p> </td><td data-bbox="654 558 1403 667"> <ul style="list-style-type: none"> Pseudo Aneurysm extravascular Pulsatile hematoma by breach in vessel wall. </td></tr> <tr> <td data-bbox="456 667 654 1045"> <p>Other Types</p> </td><td data-bbox="654 667 1403 1045"> <ul style="list-style-type: none"> Mycotic aneurysm is seen in bacterial infection. MICRO aneurysms are earliest change in Diabetic retinopathy. Berry Aneurysm (Saccular aneurysm of Circle of Willis): Lacks Tunica MEDIA no link with atherosclerosis. Frequent cause of Subarachnoid haemorrhage in polycystic kidney disease. Abdominal Aortic aneurysm: Palpable Pulsatile abdominal mass involving mainly descending abdominal aorta caused by Atherosclerosis mainly Tertiary Syphilis Involves Ascending Aorta. Tree Bark appearance (BCQ). Syphilis Involves Vasa Vasorum  endarteritis obliterans </td></tr> </table>	<p>True aneurysm</p>	<p>Involving all 3 layers of vessel/Heart e.g in syphilis, atherosclerosis, and Lt Ventricle aneurysm True aneurysm has 2 types :</p> <ol style="list-style-type: none"> Saccular (spherical outpouching) Fusiform (Circumferential) – Most common type. 	<p>False Aneurysm</p>	<ul style="list-style-type: none"> Pseudo Aneurysm extravascular Pulsatile hematoma by breach in vessel wall. 	<p>Other Types</p>	<ul style="list-style-type: none"> Mycotic aneurysm is seen in bacterial infection. MICRO aneurysms are earliest change in Diabetic retinopathy. Berry Aneurysm (Saccular aneurysm of Circle of Willis): Lacks Tunica MEDIA no link with atherosclerosis. Frequent cause of Subarachnoid haemorrhage in polycystic kidney disease. Abdominal Aortic aneurysm: Palpable Pulsatile abdominal mass involving mainly descending abdominal aorta caused by Atherosclerosis mainly Tertiary Syphilis Involves Ascending Aorta. Tree Bark appearance (BCQ). Syphilis Involves Vasa Vasorum  endarteritis obliterans
<p>True aneurysm</p>	<p>Involving all 3 layers of vessel/Heart e.g in syphilis, atherosclerosis, and Lt Ventricle aneurysm True aneurysm has 2 types :</p> <ol style="list-style-type: none"> Saccular (spherical outpouching) Fusiform (Circumferential) – Most common type. 						
<p>False Aneurysm</p>	<ul style="list-style-type: none"> Pseudo Aneurysm extravascular Pulsatile hematoma by breach in vessel wall. 						
<p>Other Types</p>	<ul style="list-style-type: none"> Mycotic aneurysm is seen in bacterial infection. MICRO aneurysms are earliest change in Diabetic retinopathy. Berry Aneurysm (Saccular aneurysm of Circle of Willis): Lacks Tunica MEDIA no link with atherosclerosis. Frequent cause of Subarachnoid haemorrhage in polycystic kidney disease. Abdominal Aortic aneurysm: Palpable Pulsatile abdominal mass involving mainly descending abdominal aorta caused by Atherosclerosis mainly Tertiary Syphilis Involves Ascending Aorta. Tree Bark appearance (BCQ). Syphilis Involves Vasa Vasorum  endarteritis obliterans 						
<p>AORTIC DISSECTION</p>	<ul style="list-style-type: none"> longitudinal intimal tear Most common cause : Hypertension > Atherosclerosis Other causes are Marfan syndrome and aneurysms etc. Sudden Severe Tearing chest Pain in HTN patients with Mediastinal widening on Chest X Ray + Unequal B.P in both arms is most likely = Aortic DISSECTION. <p><u>Classification :</u></p> <p>STANFORD A Type involves Ascending Aorta STANFORD B Type involves Des Aorta below Lt Subclavian</p>						
<p>IMP BCQS</p>	<ul style="list-style-type: none"> Hyperlipidemia > HTN is MCC of Atherosclerosis Atherosclerosis > HTN is MCC of Aneurysm HTN > Atherosclerosis is MCC of Dissection MC atherosclerotic aneurysm site is Abd Aorta MC site of peripheral aneurysm is Popliteal artery Dissecting aneurysm involves Asc Aorta mainly Traumatic aneurysm involves Des Aorta MCC of Thoracic Aortic Aneurysm is HYPERTENSION & cystic medial degeneration seen. Atherosclerosis involves Intima & Aneurysm involves Media Dissection is caused by Intimal Tear (Longitudinal) 						

VASCULITIS

- Can involve Large, Medium/Small vessel vasculitis.
- May be Granulomatous/Non-Granulomatous. Associated with systemic diseases.
- ANCA association (Pauci immune) No link with Immune complexes

Large Vessels Vasculitis	<p>Giant Cell/Temporal & Takayasu arteritis</p> <p>Giant Cell Arteritis (Temporal Arteritis):</p> <ul style="list-style-type: none"> • Adults > 50yrs old + Female mostly involves Superficial Temporal artery commonly. Polymyalgia Rheumatica association • Unilateral Temporal headache, jaw claudication and ESR raised. • Temporal artery biopsy is gold standard for diagnosing it. • On biopsy Fragmentation of internal elastic Lamina + granulomatous segmental inflammation. Treated with Steroids <p>Takayasu Arteritis:</p> <p>< 50 years old. Involves Aortic arch (Subclavian artery mostly involved). Pulseless disease. Biopsy is diagnostic</p>
Medium Vessel Vasculitis	<ul style="list-style-type: none"> • Polyarteritis Nodosa + Kawasaki + Buerger disease <p>Polyarteritis Nodosa (PAN): Hep B association in 30% + Fibrinoid necrosis Involves RENAL vessels and Sparer Pulmonary vessels. Biopsy is diagnostic: transmural inflammation seen. Lesion of all stages (old + new) can be seen (BCQ)</p> <p>Kawasaki:</p> <ul style="list-style-type: none"> • Self-limiting disease in mostly Asian (Japan) child < 4 years age. • May develop Coronary aneurysm/Rupture causing death. Present with: • Fever for 4 to 5 days with: • Rash + Cervical Lymphadenopathy + Strawberry tongue + Hand Foot edema • May cause MI in children. Anti Endothelial Ab +ve <p>Buerger Disease:</p> <ul style="list-style-type: none"> • Typical patient is 35 yr. old Male Smoker. • Gangrene of toes and auto amputation of digits
Small Vessel Vasculitis	<ol style="list-style-type: none"> 1. ANCA +ve: Microscopic Polyangiitis + Wegener + Churg Strauss syndrome 2. ANCA-Ve: Henoch Scholein purpura <hr/> <p>C-ANCA+ve (PR-3 ANCA):</p> <p>Wegener granulomatosis : Nasal + Lung's granulomas and necrotizing lesions</p> <ul style="list-style-type: none"> • Remember it by World Cup = WC → Wagner is C Anca +ve <hr/> <p>P-ANCA(MPO-ANCA)</p> <p>Microscopic Polyangiitis:</p> <ul style="list-style-type: none"> • NO Granulomas seen. • Involves LUNGS + RENAL vessels but NOT Nose. • Lesion of Same ages Present (BCQ) <hr/> <p>IMP BCQs</p> <p>Lesion of different ages Old and new together PAN and lesion of same ages in microscopic polyangiitis (BCQ)</p> <p>Churg Strauss Syndrome: EOSINOPHILIA + Asthma and P-Anca +ve.</p> <p>Remember P ANCA+VE by PMC (P+ ve) → Microscopic polyangiitis + Churg Strauss.</p>

VARICOSE VEINS

- Dilated/tortuous veins. Incompetent valves are the cause.
- SAPHENOUS Vein (20 valves) mostly involved.
- Risk factors include Age, Obesity, Pregnancy and Long Standing (Soldiers/Guards)
- Varicose veins can lead to DVT & Embolism. Duplex Scan is gold standard.
- **Thrombophlebitis** is venous thrombosis due to infection/inflammation.
- Whereas without infection/inflammation is called **Phlebothrombosis**
- Causes include Heart failure, immobilisation/Prolonged Bed rest, Varicose veins & pregnancy

ISCHEMIC HEART DISEASES / CORONARY ARTERY DISEASES

- IHDs include Angina + MI + Chronic IHD + Sudden Cardiac Death
- Major cause of Morbidity and Mortality worldwide. 90% cause of IHD is Atherosclerosis

Angina Pectoris	<p>Ischemic Chest Pain but No Myocardial Necrosis. Imbalance In Myocardial O2 Supply & Demand</p> <p>Types:</p> <ol style="list-style-type: none">Stable Chest Pain While Exertion That Resolves with Rest/ Nitro-glycerine (2mg S/L) 70-75% Vessel Occlusion by Atherosclerosis. St Depression May Be on ECG.Unstable: Chest Pain At Rest, St Depression/T Inversion. Unstable May Present with Symptoms of Angina/MiVasospastic/Prinzmetal/Variant Angina : Seen in Smokers 2ndary To Coronary Vasospasm. Transient St Elevation on ECG. <p>Note: Cardiac Markers Are Normal in Angina That Differentiates It from Mi</p> <p>Management</p> <ul style="list-style-type: none">o Goal Is Reduction of Myocardial O2 Demand by Decreasing EDV/Bp/Hr/Contractility/Mvo2o Beta Blockers & Nitrates: Dec EDV + Bp + Mvo2o Ejection Time : Beta Blockers Inc It. Nitrates Dec It.o Because Nitrates Cause Tachycardia and Heart Ejects Speedily Therefore Ejection Time Is Less While Beta Blockers Slow Down Heart Therefore Ejection Time is Raised.o Pindolol + Acebutolol Are Partial Agonist, Better to Avoid in Angina.o Ranolazine Dec Sodium Current and Used in Refractory Angina (R For Ranolazine & Refractory)					
Acute Coronary Syndrome	<ul style="list-style-type: none">• It includes Unstable Angina ,NSTEMI and STEMI• ST Depression is a feature of : Stable , Unstable Angina + NSTEMI <table><tr><th>Non-ST Elevation MI (NSTEMI)</th><th>ST Elevation MI (STEMI)</th></tr><tr><td><ul style="list-style-type: none">➤ Sub endocardial infarct Leading to necrosis of interior 1/3rd of myocardium.➤ On ECG : ST Depression with/without T inversion</td><td><ul style="list-style-type: none">➤ Transmural infarct involving endocardium to epicardium.➤ ST elevation + Cardiac Enzymes raised.</td></tr></table>		Non-ST Elevation MI (NSTEMI)	ST Elevation MI (STEMI)	<ul style="list-style-type: none">➤ Sub endocardial infarct Leading to necrosis of interior 1/3rd of myocardium.➤ On ECG : ST Depression with/without T inversion	<ul style="list-style-type: none">➤ Transmural infarct involving endocardium to epicardium.➤ ST elevation + Cardiac Enzymes raised.
Non-ST Elevation MI (NSTEMI)	ST Elevation MI (STEMI)					
<ul style="list-style-type: none">➤ Sub endocardial infarct Leading to necrosis of interior 1/3rd of myocardium.➤ On ECG : ST Depression with/without T inversion	<ul style="list-style-type: none">➤ Transmural infarct involving endocardium to epicardium.➤ ST elevation + Cardiac Enzymes raised.					
Myocardial Infarction	<ul style="list-style-type: none">➤ Myocardial Infarction (Heart Attack)➤ MI is of 2 types NSTEMI and STEMI as described Above.➤ Most common cause is Acute Coronary Thrombus. Leading cause of death in DM is MI (15%) <p>Clinical Features</p> <ul style="list-style-type: none">• Any Chest Pain > 1hr, Not Relieved by Nitro-glycerine & Nelbin should be suspected as MI, pain may be radiate to Lt Arm, Jaw & Shoulder• Chest Pain with Perspiration/Sweating Nausea/Vomiting, anxiety and SOB can be seen• Tachycardia is the First Sign, but Dyspnea is the first Symptom• Silent MI: it may happen without Chest Pain in DM and Elderly females. Neuropathy in DM predisposes to silent MI.					

	<p><u>INVESTIGATIONS:</u></p> <ul style="list-style-type: none"> ○ ECG: Best in first 06 hrs - Investigation of Choice as well in first 06 hrs ○ T Waves changes are earliest, and ST Displacements are the specific changes. ○ Cardiac Enzymes/Markers: Myoglobin, CKMB, TROP T&I, LDH and Myoglobin ○ Myoglobin: most sensitive in first 02 hrs but nonspecific ○ CKMB: used for diagnosing within 04hrs. Persists for 02 days & then falls ○ Used for RE- INFARCTION (because its levels return after 48hrs) ○ Troponin: after 04 hrs. Trop T is Most sensiTive (T in both Trop T & sensiTive) ○ Trop I is Most specific/Confirmatory & Gold standard (BCQ) ○ Trops persist for 7 to 10 days; so, cannot be used as marker for re infarction ○ LDH: Late to raise & late to go away. It is raised on 2nd day On Day 2 Trop I& LDH coexist together Cardiac imaging and angiography can also be done. <p><u>Vessels Commonly involved in MI :</u></p> <ul style="list-style-type: none"> ○ LAD > RCA > LCX. ECG is least sensitive in diagnosing LCX infarcts 	
Types Of MI based on Walls & Leads Involved	Anterior wall	<ul style="list-style-type: none"> • Lead V1-V6 and LAD involved
	Lateral Wall	<ul style="list-style-type: none"> • Lead I +avL and LCX involved
	Inferior Wall	<ul style="list-style-type: none"> • Lead II + Lead III+ avF . • RCA > Rt Marginal artery involved in inf wall MI
	Posterior wall	<ul style="list-style-type: none"> • V1-V2 Tall R+V1-V4 ST depression. RCA is involved • RCA is involved in both Inferior and posterior wall MI
Morphological Changes in MI	<ul style="list-style-type: none"> • Within 12 hrs: NO Gross changes. • 4-12 hrs: coagulative necrosis begins. • 12- 24 hrs: Neutrophils + Marginal necrosis • 1-3rd day: YELLOW tan + coagulative necrosis • 3-7 day: Macrophages infiltration • 7-10 day: RED tan + early granulation tissue • 10-14 day: well established granulation + Collagen deposition • 2-8wks: Collagen inc but cellularity dec • > 2 months: Dense Scar <p><u>IMP BCQs</u></p> <ul style="list-style-type: none"> ❖ Neutrophils present within 24 hrs and No Gross changes in 24 hrs ❖ Macrophages appear on day 3-7 	

<p>Management</p>	<p><u>MONA Therapy</u></p> <ul style="list-style-type: none"> ❖ MORPHINE : 5 mg Nelbin/Morphine IV × STAT to relieve Pain & Anxiety ❖ O2 therapy + Nitrates (Sublingual Angised 2mg) ❖ Oral Aspirin 300mg (Aspirin improves Morbidity in ACS) ❖ Inj Heparin 5000 IU IV × Stat <p><u>Definitive Treatment</u></p> <ul style="list-style-type: none"> ❖ Thrombolysis Or Primary PCI (Angioplasty) ❖ Thrombolysis by Streptokinase Best thrombolytic is Tenecteplase > Reteplase > Alteplase > Streptokinase. ❖ Angioplasty/Stenting aims at Improving Blood flow ❖ BYPASS Surgery in Triple Vessel disease and Complicated cases ❖ Door to Needle (SK) time should be < 60 min. Ideal is < 30 min ❖ Door to Balloon time (Angio) must be < 90 min. <p>Practical Tip:</p> <ul style="list-style-type: none"> ❖ Always Ask Patient for Aspirin Allergy. ❖ Always Follow ACS Protocol before Labs are available. ❖ ACS protocol: 1 Tab Aspirin 300mg +4 Tabs Clopidogrel 75mg each ×Stat ❖ Providing O2 to patients who have Dyspnea is Prominent & keep in Mind the differentials of MI: Pulmonary Embolism + Pneumothorax + Rupture of Oesophagus/Perforated Duodenal Ulcer. ❖ Chest pain is mostly present but Not Universal as Inferior wall MI can present with Abdominal Pain too
<p>Complications</p>	<ul style="list-style-type: none"> • Arrhythmias: MCC of death in 24hrs (V fib most common) • Death in 1st hr: V fib is the cause • Death after 1st hr: SVT may be the cause • 1-3 Days: Fibrinous Pericarditis • 4- 7 days: Cardiac Tamponade by Rupture of Vent free wall/ intervent septum/ Papillary Rupture → Mitral regurgitation (MR) • Months post MI: Ventricular Aneurysm • MC Late complication is Vent Aneurysm • Dressler Syndrome: Autoimmune Pericarditis following 2 months post MI <p><u>NOTE</u></p> <ul style="list-style-type: none"> • MC Valvular Lesion post MI is Mitral Regurge (MR) • COCAINE MI: Normal Coronaries + Contraction Band Necrosis • Reperfused Infarct: inc Ca causes Hypercontraction of Sarcomeres → Contraction Band necrosis. • ST Elevation is a feature of: Prinzmetal angina + STEMI

VALVULAR DISORDERS

- 4 Valves → AV Valves : Mitral + Tricuspid and Semilunar : Aortic + Pulmonary
- Diseases Mostly affect Mitral > Aortic Valve
- Tricuspid valve involved more in interventricular septal disease
- Valvular Disorder Can be either Stenosis (narrowing) or Regurge (insufficiency)
- In TOF, prominent Murmur is of Pulmonary valve stenosis.
- In pregnancy Mitral stenosis gets severe (BCQ)
- Murmur is an abnormal sound heard on auscultation when blood passes through stenosis/ Regurgitant valves.
- There are 6 grades of Murmur. Stage 4 murmur is called Thrill may be palpable .
- Innocent Murmur present in Thyrotoxicosis
- Continuous machinery Murmur(Gibson Murmur) : in PDA e.g Congenital Rubella/ mothers living in Hilly Areas.
- Prematurity – risk factor for PDA
- Gold standard diagnosis of valvular diseases by ECHO
- Trans esophageal ECHO and Trans thoracic ECHO used. Prefer Trans thoracic echo
- Learn MS +MR + AS by Heart as most BCQs are about them. Focus more on Cause + type & Site of Murmur.

MITRAL VALVE

(4-6cm² normal orifice)

Mitral Stenosis	<ul style="list-style-type: none"> • narrowing of orifice < 2.5 cm². MCC is RHEUMATIC Heart disease • Presents with Dyspnea, Hemoptysis And rarely Dysphagia due to LA dilatation. • MURMUR: MID DIASTOLIC + Opening Snap. Murmur heard at Left 5th ICS in MCL. • For Mitral Stenosis, Severity depends on LENGTH of Diastolic Murmur. • Loud S1 is heard (also present in Tachycardia). Other imp Features: • Left Atrial dilatation, Pulmonary HTN and Rt Vent Hypertrophy • Indication of Mitral valve replacement = Floppy Valve > Ruptured Chordae tendinae.
Mitral Regurgitation	<ul style="list-style-type: none"> • MCC is Mitral Prolapse (e.g seen in Marfan syndrome) • Postero Medial Papillary Rupture 2nd common cause. • Volume overload occurs due to insufficiency & back flowing blood leads to ECCENTRIC LVH • Presents with Cough, dyspnoea & Insp crackles • MURMUR: Pansystolic Murmur with S3+S4. Gallop present • Murmur may radiate to Axilla and Heard in Lt 5th ICS MCL
Mitral Valve Prolapse	<ul style="list-style-type: none"> • mostly female pt /Marfan syndrome. Also called Floppy Valve. • Characteristic change is MYXOID Degeneration (BCQ) (inc Dermatan sulphate & GAGs) • MIDSYSTOLIC Click present (BCQ) • For Mitral prolapse : Remember: Marfan + Myxoid degeneration and Mid systolic click

AORTIC VALVE

Aortic Stenosis	<ul style="list-style-type: none"> • Normal orifice is 3 cm². • < 1cm² orifice of aortic valve is known as stenosed. if < 0.5cm² it is severe AS • Cause in Old age is calcification. • While in Young around 30 it is caused by BICUSPID aortic valve (also in Turner syndrome) • Typical patient is old age 60/70s with syncope / angina/ Heart failure symptoms. • slow rising pulse & Narrow Pulse Pressure is also present. • Slow rising pulse in AS also called Pulsus parvus et Tardus. • Murmur: Ejection systolic Murmur that may radiate to Neck/carotids • Murmur heard at RIGHT 2nd ICS > 3rd ICS. Soft S2 & S4 present
Aortic Regurgitation	<ul style="list-style-type: none"> • Rheumatic Fever is MCC. • Also caused by dilatation of Asc Aorta due to HTN and aging.

	<ul style="list-style-type: none"> Incompetent closure causes backflow of blood and leads to eccentric LVH Presents with EARLY Diastolic Murmur + S3/S4. Murmur heard at RIGHT 2nd ICS (aortic area) Wide Pulse Pressure in AR (Narrow in AS) (BCQ) Narrow pulse pressure is present in AS & wide PP in AR. BOUNDING PULSE (Corrigan water hammer Pulse) if options of both Bounding Pulse & Early Diastolic Murmur. Prefer Early diastolic Murmur. Other features due to Hyperdynamic Circulation are as follows : PISTOL shot femoral (Duroziez sign), Pulsating Nail Bed (Quincke's sign, Pulsating Uvula Head Nodding (Mussel sign) Austin Flint Murmur : Mid diastolic Murmur present in severe AR
TRICUSPID VALVE	
Tricuspid Regurgitation	<ul style="list-style-type: none"> MCC is Functional. Infective endocarditis in IV drug abusers and Carcinoid syndrome. Pansystolic Murmur tricuspid area Lt 4th ICS lateral to sternum. pulsating Liver + Giant V wave on JVP
Tricuspid Stenosis	<ul style="list-style-type: none"> Mid diastolic Murmur Prominent A wave Slow Y descent on JVP
PULMONARY VALVE	
Pulmonary Regurgitation	<ul style="list-style-type: none"> Mostly Functional murmur. Pansystolic type of murmur Graham Steel Murmur: Early diastolic Murmur in PR
Pulmonary Stenosis	<ul style="list-style-type: none"> Ejection systolic Murmur. A Feature of Carcinoid syndrome is PS. Remember in Carcinoid syndrome: TR + PS murmurs present. Carcinoid involves Rt Side of heart. Lt sided involvement is seen in Patent Foramen Ovale.

PAN SYSTOLIC MURMUR	EJECTION SYSTOLIC	MID DIASTOLIC	EARLY DIASTOLIC
MR, TR , VSD	AS , PS , ASD	MS , TS	AR , PR

How To Remember It Theoretically :

- Pansystolic is ↔ with Mid diastolic**
- Ejection systolic is ↔ with Early diastolic.
- Mitral & tricuspid pair & aortic pair with Pulmonary.
- Now, only Remember PANSYSTOLIC → MR, TR,VSD & Its other counterpart will be Mid diastolic → MS, TS.
- To memorise Aortic; a & e are vowels in alphabet. So Early diastolic and Ejection systolic correspond to Aortic Valve. Clinically one can learn them with practice & skill.

Clinically imp Point

- Rt sided Murmurs inc with Inspiration (VR & preload raises) and Lt sided inc with Expiration.**
- Hand Grip inc Lt sided Murmurs.
- Valsalva dec most Murmurs by dec Preload.
- Passive Leg raise + Squatting inc Most Murmurs due to inc Preload & TPR
- Squatting or Knee to Chest position is helpful in TOF by increasing TRP/SVR**

CARDIOMYOPATHIES

- Mainly divided into 3 types Dilated, HOCM and Restrictive)
- NO association with HTN, IHD, Congenital heart diseases, valvular disorders & inflammation.
- May cause Systolic / Diastolic Dysfunction
- Systolic dysfunction in Dilated Cardiomyopathy. Diastolic dysfunction in HOCM and Restrictive
- Most common is Dilated type But in Athletes/young people sudden cardiac death seen in HOCM.
- Never give ACE inhibitors or nitrates/ digoxin in HOCM

Dilated Cardiomyopathy (Congestive)	<ul style="list-style-type: none"> • Displays Eccentric hypertrophy (sarcomeres in series) & Systolic dysfunction. • Global enlargement of Heart seen. MCC is Idiopathic or coronary artery disease. • Other risk factors are B1 def (beriberi), Alcohol. Doxorubicin induced. • Findings: MR+S3+ HF. Balloon shaped heart on x ray • Treat With ACE inhibitors, ARBs, Diuretics, and beta blockers.
Hypertrophic Obstructive Cardiomyopathy (HOCM)	<ul style="list-style-type: none"> • Hypertrophy occurs but no dilatation of heart. • Diastolic dysfunction with greater hypertrophy of interventricular membranous septum. • B myosin Heavy chain mutation found commonly. • Concentric Hypertrophy → Sarcomeres in parallel. • Syncope in young/ athletes during exertion & SCD. • Findings: MR + Systolic anterior motion of Mitral leaflet. Jerky Pulse + Palpable Double Apical Impulse. Asymmetric Hypertrophy with aberrant myofibrils • Myocytes disarray seen. Binucleation present. • Perivascular, interstitial and replacement fibrosis. • Treat by Beta blockers - 1st line > Ca channel blockers • Avoid Diuretics, ACE inhibitors & drugs decreasing Preload.
Restrictive Cardiomyopathy	Diastolic Dysfunction. Amyloidosis is MCC followed by Hemochromatosis. Rare causes are Sarcoidosis, Radiations and Pompe disease Can Lead to Biventricular failure. Treatment is Heart Transplant

Takotsubo Cardiomyopathy (Broken Heart Syndrome):

- Stress cardiomyopathy linked to strong Emotional & physical experience.
- Shape of the LV becomes like an Octopus Trap.

CONGENITAL HEART DISEASES

Cyanotic Heart Diseases (R → L Shunt)	<ul style="list-style-type: none"> • Blue babies • These diseases Include TOF ,TGA ,Tricuspid atresia, Truncus arteriosus and Ebstein anomaly • In R to L shunt, cyanosis occurs because Right Side of the heart receives deoxygenated blood
Acyanotic Heart Diseases (L → R Shunt)	<ul style="list-style-type: none"> • Frequency of Acyanotic diseases : VSD > ASD > PDA • NO shunts present in Coarctation of Aorta. • L to R shunts .cause late cyanosis (e.g PDA)
Remember the shunts Like:	Right to Left → eaRLy cyanosis (letter RL together) Left to Right → LaterR cyanosis

ACYANOTIC HEART DISEASES (L → R SHUNTS)	
They Result in Pulmonary HTN & Eisenmenger syndrome (finally conversion of L to R into R to L shunt)	
Ventral Septal defect	<ul style="list-style-type: none"> MC Overall CHD. MC in Children also 25%. MC defect lies in Membranous interventricular septum. Pansystolic Murmur at Left Lower Sternal Border is a feature of VSD Or Harsh Holosystolic murmur in whole precordium. VSD Presents with : Recurrent infections and Failure to Thrive. May be Asymptomatic throughout Life if of smaller size. Small defects close spontaneously. large ones require surgical closure.
Atrial Septal defect	<ul style="list-style-type: none"> MC in Adults . Females > Males. Can be Asymptomatic Ostium Secundum defect is More common -- patent Foramen Ovale. Presents with : Recurrent Chest infections, Exertional dyspnea, or Intolerance to Exercise. Fixed Splitting of S2. ASD May cause paradoxical embolism
Patent ductus arteriosus	<ul style="list-style-type: none"> failure of closure of fetal ductus arteriosum. found in Congenital Rubella syndrome and Hypoxic conditions e.g., Hilly Areas. PDA is normal feature in Utero and must close after birth PDA is Closed with INDOMETHACIN. PGE2 maintains patency during fetal life ECG is Normal in PDA
Coarctation of Aorta	<ul style="list-style-type: none"> May be Pre ductal or post ductal. 70% infantile pre-ductal type associated with Turner syndrome and Bicuspid Aortic Valve. 30% Post ductal: distal to Ligamentum arteriosum or narrowing of aorta distal to origin of Subclavian artery. Post ductal presents with inc BP in Upper Limbs than Lower Limbs Systolic Murmur in Upper sternum or Interscapular region and Radio-femoral delay On X Ray : inverted 3' sign due to rib Notching caused by development of Collaterals.
Eisenmenger syndrome	<ul style="list-style-type: none"> Uncorrected L To R reverses to R to L shunt due to Pulmonary HTN Remodelling of Pulmonary Vasculature leads to Pulmonary HTN
CYANOTIC HEART DISEASES (R → L SHUNTS)	
Tetralogy of Fallot	<ul style="list-style-type: none"> MC Cyanotic disease is TOF. Tetra means 4, so 4 Anomalies in TOF can be Remembered by mnemonic: PROVe → Pulmonary stenosis + RVH + Overriding aorta + VSD Boot shaped heart seen on CXR Features of TOF : Tet Spells/ Hypoxemic Spells: Sudden inc in HYPOXEMIA & CYANOSIS due to Crying, Fever/Anaemia. SQUATTING ↑ systemic Vascular Resistance. Causes temporary Reversal of Shunt from R To L → L to R. Murmur is harsh systolic (from Pulmonary stenosis & RV outflow obstruction) Clubbing, Cyanosis, Failure of Thrive, Polycythemia and relative Anaemia due to hypoxemic states. Treat Tet spells with O2 + Morphine and knee to chest position Oral Propranolol may be used for prophylaxis and management of Tet spells Definitive Treatment Includes correction of Surgical anomalies if conditions allows or Palliative surgery by Balock Tausig operation → Shunt + anastomosis b/w subclavian & Pulmonary artery. Ideal age for Surgery is <1 Yr. (but can be done 1-5yrs)
Transposition of Great arteries	<ul style="list-style-type: none"> Most common cause of cyanosis at Birth. Abnormal formation of Truncal + Aortico - Pulmonary septum i.e Aorta arises from RV (anterior) & Pulmonary artery from LV (posterior) Egg on string appearance on CXR. Shunt is necessary for Survival (PDA/VSD) Infant of Diabetic Mother may have TGAs
Tricuspid atresia	<ul style="list-style-type: none"> Absence of tricuspid valve it Requires both ASD + VSD for survival.
Truncus arteriosus	<ul style="list-style-type: none"> Lack of Aortico Pulmonary Septum formation here (abnormal in TGA) Most pts have coexisting VSD
Ebstein anomaly	<ul style="list-style-type: none"> Low lying Tricuspid Leads to small Ventricle and Large Atrium. H/o Lithium Exposure during pregnancy. Also known as Arterialization of RV

HEART FAILURE

- Cardiac Remodelling due to hemodynamic and neuro-hormonal stressors lead to reduced CO.
- Compensated HF:** Force of contraction is decreased but with mild symptoms or no symptoms at all.
- Decompensated HF:** FOC is dec further resulting in clinical signs & symptoms.
- HF may be Right HF /Lt HF or maybe both.
- Right HF gives Signs while LHF gives Symptoms.**
- Congestive HF/CCF** is failure of LHF/RHF or both.
- HFrEF = HF with reduced ejection Fraction. HFpEF = HF with preserved EF
- EF Normal 55 to 65% or 0.55-0.65.
- Systolic dysfunction (HFrEF)** = HF with reduced EF < 55%. Often results from MI / dilated cardiomyopathy.
- Diastolic dysfunction = HFpEF** (EF is preserved) often 2ndry to Myocardial Hypertrophy e.g HTN/ HOCM

Facts To Remember

- Reduced Contractility in Systolic HF whereas Reduced Compliance in Diastolic HF.
- Hypercalcemia & hypokalemia cause Systolic arrest. Hyperkalaemia & Hypocalcaemia cause Diastolic arrest.
- ANP is released from Atria & BNP from Ventricles. BNP > ANP is more specific for Heart failure.
- BNP raised helps to differentiate from other causes of dyspnea like Asthma & Pulm HTN etc.
- Failure of Rt Heart due to Lt Heart is = CCF / Congestive Cardiac failure. MCC of LHF is IHD (Especially MI)
- MCC of RHF is LHF. If LHF not in options, then Prefer Pulmonary HTN > COR – PULMONALE.
- Severe LVF can lead to Pulsus Alternans (weak & strong beat alternates).
- O2 sat is 100% in LA + LV + Aorta. O2 sat is 70% in RA+ RV + pulmonary Artery.

Left Heart Failure	<ul style="list-style-type: none"> ○ Acute form is called Pulmonary Edema Causes: IHDs (MI) are the leading cause. ○ Also, HTN and valvular disorders along with Cardiomyopathies contribute to LHF. ○ Pulmonary Edema → Hemosiderin Laden macrophages (HF cells present) ○ Paroxysmal Nocturnal Dyspnea (PND) : SOB while sleeping awakes Pt . due to inc VR & Preload is an imp feature of LHF Orthopnea → SOB while Lying. Cough, hemoptysis & distended neck Veins. ○ Both PND + Orthopnea relieve while sitting Upright S3 or sometimes S4 present ○ Management by: LMNOP → Loop Diuretics, Morphine, O2, Nitrates, Propranolol.
Right Heart Failure	<ul style="list-style-type: none"> ○ Signs include Edema , Hepatomegaly, Raised JVP ○ Chronic Passive Hepatic Congestion in CCF leads to Nutmeg (mottled) appearance of Liver
Role of Drugs	<ul style="list-style-type: none"> ○ Drugs improving/ decreasing Mortality in HF → ACE inhibitors and Spironolactone. ○ Vasodilators e.g Nitrates, Hydralazine and Beta blockers Reduce Both Mortality + Symptoms. ○ NOT Improving MORTALITY → Diuretics + Digoxin and Ca channel blockers ○ Nesiritide → INCREASED Mortality ○ Drugs In Acute HF → Diuretics , Beta agonist and Vasodilators ○ Drugs In Chronic HF → ACE inhibitors , Beta Blockers ,Vasodilators and Digoxin ○ Beta blockers effective Chronic Stable HF or Chronic Systolic HF ○ NEVER give BETA blockers in Acute HF as they may worsen it. ○ Always rule out Asthma before giving Beta-blockers
Digoxin	<ul style="list-style-type: none"> ○ It is used in HF + A fib or CCF. ○ It blocks Directly Na - K ATPase pump. ○ Indirect inhibition of Na Ca exchangers ↑ intracellular Ca⁺ ○ Inc FOC (+ve Inotropy). DIGOXIN inc Force of contraction but Heart rate decreases ○ Side effects: Nausea/Vomiting /diarrhoea are most common in it. Yellow vision/ AV blocks. <p><u>Toxicity of Digoxin</u></p> <ul style="list-style-type: none"> ○ Hyperkalaemia. <p>Toxicity is made worse if there is Pre-existing Hypercalcemia or Hypokalemia</p>

	<ul style="list-style-type: none"> Reason: Digoxin competes with K⁺ for Na-K ATPase. If there is already Low K⁺ level then it binds more and more, hence more toxicity occurs. It inc Ca Levels; if there is already Hypercalcemia; then toxicity is more. Anti Dote is Digi – Fab slowly Normalize K⁺ and, also give Mg⁺² in toxicity.
--	---

RHEUMATIC FEVER	
<p>A Multisystem inflammatory disease Caused by Group A beta hemolytic Streptococci After Sore Throat > Skin infection (cellulitis). Age 5 to 15 yrs. mostly. Immune mediated Type 2 HS reaction.</p> <p>Mitral and Aortic valves affected more commonly.</p> <p>Molecular Mimicry:</p> <p>Antibodies against M proteins cross react with glycoprotein Ag in Heart, Joints and other tissues is the pathogenesis</p>	
Diagnosis	<ul style="list-style-type: none"> JONES criteria as follows: 2 Major Criteria OR 1 Major + 2 Minor is diagnostic along with raised ASO & throat culture. Major Criteria: Joint involvement + Carditis + Nodules + Erythema Marginatum and Chorea Minor Criteria: Fever + inc ESR + inc TLC, Arthralgia, prolonged PR interval on ECG. Initial Test: Raised ASO titres (1:80 raised is diagnostic) Best diagnostic: Throat culture > Blood culture
Microscopic findings	<ul style="list-style-type: none"> Aschoff Bodies → Fibrinoid necrosis seen, early finding Anitschkow cells are slender, wavy chromatin - ribbon like. McCullum plaques formed due to irregular LA wall thickening.
Imp Facts	<p>Pancarditis (with bread & butter pericarditis) is seen in this disease</p> <p>MCC of death is Myocarditis > CCF in Acute cases.</p> <p>Migratory Polyarthrititis is most commonly present.</p> <p>Chorea/ Sydenham chorea is Late finding or may be the only finding in some cases</p> <p>Acute RF → Mitral Regurge.</p> <p>Chronic RF → Mitral Stenosis (fish mouth/Buttonhole deformity)</p>
Management	<p>Medical + Surgical to Eradicate infection:</p> <p>Single IM dose of 1.2M Units of Benzyl Penicillin,</p> <p>In children < 20kg : 0.6M units IM</p> <p>Oral Penicillin V 500 mg B.d 10 days.</p> <p>In Penicillin allergy : Erythromycin 500mg 1 × B.d × 10 days</p>
Prophylaxis	<ol style="list-style-type: none"> RF without Carditis : for 5yrs/ 21yrs of age (whichever Longer) RF + Carditis + no Valve disease : for 10yrs or 21yrs age RF + Carditis + Valvular disorder : 10yrs or 40yrs age/Lifelong sometimes
Complications	Endocarditis ,CCF ,embolism, Arrhythmias, and death

Infective Endocarditis	<ul style="list-style-type: none"> ❖ Large bulky friable irregular Vegetations on valves ❖ Triad of Fever + Murmur + Splenomegaly ❖ H/o Dental Surgery mostly present. ❖ Mitral + Aortic valve affected more. 				
Causes	<ul style="list-style-type: none"> ❖ Bacterial: Gram+ve (98% cases) ❖ MC Overall cause = Strep Viridians ❖ MCC in Subacute = S.Viridians ❖ MCC in Acute IE = Staph Aureus ❖ MCC of Rt sided & IV drug abusers is S. aureus. ❖ Culture -ve endocarditis in coxiella burnetii ❖ (only 1 culture +ve is diagnostic) ❖ PROSTHETIC Valve: Staph Epidermidis (< 60 days) ❖ Overall, for Prosthetic valves most common ❖ Staph Aureus (> 60 days) in prosthetic material infection 				
Clinical features	<ul style="list-style-type: none"> ❖ Fever is most consistent Sign of IE (BCQ) ❖ Other features: New murmur, Osler Nodes, Roth spots ❖ Janeway lesion (Painless on palm, soles): Septic Emboli ❖ Osler nodes (Painful on tips of toes/fingers: Immune mediated ❖ Roth spots are retinal haemorrhage. ❖ (While Rose spots are in Typhoid fever on 7th day) ❖ Sequence of Valve Damage is D-TBP ❖ Damaged Valve, Thrombus, Bacteraemia, Perforation 				
Diagnosis & Management	<ul style="list-style-type: none"> ❖ Blood Culture is gold standard. (BCQ) 3 sets of culture within 60-90 mins followed by antibiotics. ❖ Modified DUKE's Criteria ❖ For definitive diagnosis = 2 major or 1 Maj + 2 Minor Or 5 Minors <table border="1"> <tr> <td>Major</td><td> <ul style="list-style-type: none"> ✓ Blood Culture ✓ ECHO ✓ New Valvular regurgitation </td></tr> <tr> <td>Minor</td><td> <ul style="list-style-type: none"> ✓ Fever ✓ Vascular/Immune phenomenon ✓ Serological or microbiological evidence of Infection. </td></tr> </table> <ul style="list-style-type: none"> ✓ Penicillin (Ampicillin) + Gentamicin 4 to 6 hourly for 6-8 weeks. ✓ Prophylaxis: Amoxicillin > Ampicillin ✓ Amoxil 2gm oral / IV single dose 30 min before dental procedures. ✓ In penicillin Allergy -- Clindamycin: 600 mg Oral /IV single dose 30 min before surgery. 	Major	<ul style="list-style-type: none"> ✓ Blood Culture ✓ ECHO ✓ New Valvular regurgitation 	Minor	<ul style="list-style-type: none"> ✓ Fever ✓ Vascular/Immune phenomenon ✓ Serological or microbiological evidence of Infection.
Major	<ul style="list-style-type: none"> ✓ Blood Culture ✓ ECHO ✓ New Valvular regurgitation 				
Minor	<ul style="list-style-type: none"> ✓ Fever ✓ Vascular/Immune phenomenon ✓ Serological or microbiological evidence of Infection. 				
Complications	CCF, Shock , Stroke , Emboli and Death				
Key facts	<p><u>Vegetations:</u></p> <ul style="list-style-type: none"> ○ Large, friable, and irregular/bulky in IE ○ Small and Flat in SLE/Libman sacks ○ Small and friable in NBTE/MARANTIC type ○ Sterile Vegetations in SLE + NBTE 				
Non- Infective Endocarditis					
<ul style="list-style-type: none"> ○ Liebmansacks: Seen in SLE; MITRAL> AORTIC Sterile, Small, flat verrucous lesions are seen. ○ Marantic/ non-bacterial thrombotic Endocarditis(NBTE) : Marantic means Wasting (as wasting occurs in cancers) Terminal Neoplasm > autoimmune diseases. ○ Hypercoagulable states produced by Cancers. ○ Vegetations are Small & friable and Sterile (non-infectious) 					

PERICARDITIS

- Pericardium is divided into 2 layers = Inner Serous + Outer Fibrous layer
- Serous has further 2 layers → Parietal & Visceral.
- Visceral layer of serous is called Epicardium(BCQ)
- So Pericardial cavity is b/w Serous & Fibrous (OR) B/w Fibrous layer & Visceral Layer of Serous
- Pericardium is Supplied by PHRENIC Nerve mainly (fibrous layer)
- Visceral layer (Epicardium) supplied by VAGUS nerve.
- Pericardiophrenic artery (branch of internal thoracic) supplies blood to pericardium.
- Remember : P for pericardium & Phrenic/ pericardiophrenic artery.
V for Visceral & Vagus Nerve.

Causes	<ul style="list-style-type: none"> • Infectious/ non-infectious (autoimmune, malignancy) • Idiopathic / Viral is MCC. IDIOPATHIC > Viral • Chronic/ Constrictive/ Fibrinous pericarditis: Most common cause is Tb. • Trauma, Neoplasm, Scurvy causes Hemopericardium (BCQ) • Obstruction of SVC / Thoracic duct → CHYLOpericardium • Renal failure, Viral infections, Tumours, HF → Pericardial effusion • SLE pericarditis is one of main findings in SLE
Types Of Pericarditis	<p>Pericarditis may be Acute, Chronic and Recurrent. Pericardial effusion may be serous, Fibrinous, and hemorrhagic.</p> <ul style="list-style-type: none"> • Serous (Viral inf) • Fibrinous (Uremic / T.B) -- BCQ • Haemorrhagic (Scurvy) -- BCQ
Findings	<ul style="list-style-type: none"> • ECG in Pericarditis → PR depressions are most specific. • ECG of pericardial effusion shows electrical Alternans. • Widespread ST Elevations of saddle type seen in pericarditis. • JVP is raised. <p><u>Kassmaul sign</u></p> <ul style="list-style-type: none"> ○ Paradoxical rise in JVP during Insp, normally JVP falls on inspiration. ○ Seen in Constrictive Pericarditis > RHF, Pulm Embolism ○ Remember Kassmaul Breathing is seen in DKA
Management	<ul style="list-style-type: none"> ○ Treat underlying cause and symptomatic Rx by Aspirin/ indomethacin/ immunosuppressant like Cycloserine. ○ Surgically by Pericardial stripping
Summary	<ul style="list-style-type: none"> • Typical Pt of Pericarditis having Sharp chest Pain related to inspiration; relieved by sitting up / leaning forward • Multiples causes being Idiopathic/ viral common for acute pericarditis and Tuberculosis for chronic/ fibrous/ constrictive • PR depression > widespread ST elevation is specific. • Treat with Immunosuppressants and NSAIDs

Cardiac Tamponade	<ul style="list-style-type: none"> Fluid around heart can be effusions/blood Features : BECK's triad <ul style="list-style-type: none"> BP + JVP raised + muffled heart sounds Pulsus Paradoxus : normally during inspiration Bp falls; if BP falls >10 mmhg during Insp it is P. paradoxus , also seen in pericarditis/asthma. On ECG: Electrical alternans. voltages inc and dec due to fluid around also seen in pericardial effusion ECHO is diagnostic for Cardiac Tamponade and effusion Shows global enlargement of heart. Management by PERICARDIOCENTESIS – Treatment of choice Subxiphoid /subcostal best approach for draining fluid Other include Needle directed at 5th ICS lateral to sternum.
Myocarditis	<ul style="list-style-type: none"> Inflammation of Myocardium with global heart enlargement. FEVER + Tachycardia + dyspnea + Chest pain and Bi ventricular CHF Major cause of SCD in < 40 yrs adults COXSACKIE virus is the Most common cause Lymphocytic infiltrates + focal necrosis indicates Viral cause. Other causes are Adenovirus , HIV , Rheumatic fever; bacterial- diphtheria, Mycoplasma, Lyme disease by Borrelia & parasites (Toxoplasma Gondii & Trypanosoma Cruzi) Drugs like Cocaine + doxorubicin. Autoimmune like SLE, Sarcoidosis + Kawasaki disease. Recently, SARS COV-2 (Coronavirus) came as a known cause of it. Complications: Sudden death, Heart blocks, arrhythmias + emboli + Dilated Cardiomyopathy

CARDIAC & VASCULAR TUMOURS

- Metastatic tumours are MC overall e.g Melanoma
- PERICARDIUM is the MC site of Metastasis.
- Primary Tumours: MC 1° malignancy is ANGIOSARCOMA.
- 1° tumours are less frequent than metastatic tumours i.e MC tumors of heart are metastatic

Myxoma	<ul style="list-style-type: none"> benign + MC 1° tumour of heart, produces IL-6. Gelatinous material causes Ball Valve obstruction. Lt Atrium is the most common site. More frequent in adults. Produces tumour plop sound & early diastolic murmur.
Rhabdomyosarcoma	MC Primary Tumour in CHILD – in ventricles. MC in VENTRICLES (RV) → Hamartomatous growth.
Spider Telangiectasia	Inc Estrogenic states seen in CLD/ Pregnancy on Face. Blanching is a feature.
Kaposi Sarcoma*	Malignant vascular tumour Associates with HHV-8 in HIV

	<p>Most common site is HEAD & NECK Purple/ violaceous lesion seen containing dilated endothelial channels.</p> <p>Types: Epidemic Type : In AIDS (lymph nodes + Organs involved) Endemic/ African: NO skin lesions , Only Lymph Nodes involved Classic/ Chronic/European : Only SKIN lesions. Immunosuppressants/ Transplant related type involves LN + Mucosa + Organs.</p>
Haemangioma	<ul style="list-style-type: none"> • MC Vascular tumour of Infancy. • Responsible for Port- Wine stain birthmarks • Cavernous: occur in Liver/ Spleen commonly. • Capillary : MC type in Skin and Viscera e.g Strawberry Haemangioma. Regress itself by 07 yrs. age
Pyogenic Granuloma	<ul style="list-style-type: none"> • Cap haemangioma in Pregnancy 1%. Present on Gingiva
Hemangiopericytoma	<ul style="list-style-type: none"> • On Thighs/ Pelvic Peritoneum. • Capillaries in Fishhook pattern. Ag stain used
Hereditary Hemorrhagic Telangiectasia	<ul style="list-style-type: none"> • Also called Osler weber rendu syndrome , autosomal dominant disorder • blanching lesions of skin & mucous membranes with Recurrent Epistaxis • Characteristic lesion is on Lips (BCQ)

HYPERTENSION						
(BP Equal or >140/90 mmHg)						
Categories of BP and Stages of HTN	<ul style="list-style-type: none">At Least 3 readings of inc BP on different occasions are required for labelling a person Hypertensive.BP Categories:<table><tr><td>Healthy: <120/80mmHg</td></tr><tr><td>Elevated BP : 120-129/<80mmHg</td></tr><tr><td>Stage 1 HTN :130-139/80-89mmHg</td></tr><tr><td>Stage 2 HTN : equal or >140/90mmHg</td></tr><tr><td>HTN Crisis : B.P >180/120mmHg</td></tr></table>	Healthy: <120/80mmHg	Elevated BP : 120-129/<80mmHg	Stage 1 HTN :130-139/80-89mmHg	Stage 2 HTN : equal or >140/90mmHg	HTN Crisis : B.P >180/120mmHg
Healthy: <120/80mmHg						
Elevated BP : 120-129/<80mmHg						
Stage 1 HTN :130-139/80-89mmHg						
Stage 2 HTN : equal or >140/90mmHg						
HTN Crisis : B.P >180/120mmHg						
Types of Hypertension	<ul style="list-style-type: none">Primary or Essential HTN : Unknown aetiology, Genetic factors, salty diet, stress, smoking, and sedentary lifestyle.Secondary HTN : Having a cause -- MC are RENAL causes Including RENAL artery stenosis (common), Polycystic kidneys , Renin producing tumors & CKD.Renal artery stenosis is MC known cause 2ndry HTN.High Renin levels in stenosed vessel (BCQ) Associated with FIBROMUSCULAR Dysplasia especially in females.Avoid ACE inhibitors in RAS .Others causes of 2ndry HTN :Endocrine: Conns syndrome/Pheochromocytoma, pregnancy induced.CVS: Coarctation of Aorta, Polyarteritis NodosaCNS: psychogenic , anxiety ,stress, sleep apnea					
Hypertensive Emergency Vs HTN Urgency	<ul style="list-style-type: none">BP > 180/120 in both.May also rise to even > 220/120					

	<ul style="list-style-type: none">○ Target organs for damage -- Retina & kidney mainly○ Target organ damage (TOD) seen in HTN emergency○ IF No TOD -- Then it is HTN Urgency.						
Malignant HTN	<ul style="list-style-type: none">○ Malignant HTN is more severe -BP > 220/120 mmHg.○ Retinal Hemorrhages+ Flea bitten shaped kidneys that are swollen having punctate hemorrhages.○ Fundoscopy must be done -- Papilledema Is seen						
HTN in Pregnancy	<p><u>Gestational HTN</u></p> <ul style="list-style-type: none">○ BP >140/90 first time during pregnancy after 20wks of pregnancy (Without PROTEINURIA)○ Returns to Normal 12 weeks post- partum (transient HTN)○ Treatment : Labetalol > Methyldopa.○ IV Hydralazine in HTN Emergency in pregnancy <p><u>Chronic HTN In Pregnancy</u></p> <ul style="list-style-type: none">○ B.P > 140/90 pre pregnancy or before 20 weeks of pregnancy. Persists even after 12 weeks post-partum						
Measurement of BP	<ul style="list-style-type: none">○ Direct/ intra-arterial method is Most accurate method.○ 20-gauge catheter is ideal for child & adults (BCQ)○ 22 gauge for infants & paediatrics○ Auscultatory method : A cuff is used.○ Korotkoff sounds are caused by turbulent blood flowing through Brachial artery.○ Cuff size should be at least 80% of arm circumference or 0.5- 0.8 times the size of Arm						
Management Of HTN	<p><u>LIFESTYLE MODIFICATIONS</u></p> <table><tr><td><ul style="list-style-type: none">• Exercise 180 min/week</td></tr><tr><td><ul style="list-style-type: none">• Weight Reduction is effective in young & Middle Ages</td></tr><tr><td><ul style="list-style-type: none">• Reduce salt in diet. Prefer DASH diet</td></tr><tr><td><ul style="list-style-type: none">• DASH = Diet approaches to stop HTN, includes 5 components<ul style="list-style-type: none">🍷 Grains 6 to 8 servings🍷 Fruits & Vegetables (4 to 5 servings each day)🍷 Nuts seeds (4 to 5 servings/week).🍷 Low fat dairy products : six 1-ounce serving/day</td></tr></table> <p><u>PHARMACOLOGICAL</u></p> <ul style="list-style-type: none">○ If < 55yrs age : A+D (ACE inhibitors + Diuretics)○ If > 55yrs age : B+C (beta blockers + Ca blockers)○ For Essential HTN : ACE inhibitors , ARBs , Thiazides and Ca blockers can be used.○ Do not use Beta Blockers in decompensated HF	<ul style="list-style-type: none">• Exercise 180 min/week	<ul style="list-style-type: none">• Weight Reduction is effective in young & Middle Ages	<ul style="list-style-type: none">• Reduce salt in diet. Prefer DASH diet	<ul style="list-style-type: none">• DASH = Diet approaches to stop HTN, includes 5 components<ul style="list-style-type: none">🍷 Grains 6 to 8 servings🍷 Fruits & Vegetables (4 to 5 servings each day)🍷 Nuts seeds (4 to 5 servings/week).🍷 Low fat dairy products : six 1-ounce serving/day		
<ul style="list-style-type: none">• Exercise 180 min/week							
<ul style="list-style-type: none">• Weight Reduction is effective in young & Middle Ages							
<ul style="list-style-type: none">• Reduce salt in diet. Prefer DASH diet							
<ul style="list-style-type: none">• DASH = Diet approaches to stop HTN, includes 5 components<ul style="list-style-type: none">🍷 Grains 6 to 8 servings🍷 Fruits & Vegetables (4 to 5 servings each day)🍷 Nuts seeds (4 to 5 servings/week).🍷 Low fat dairy products : six 1-ounce serving/day							
Specific indications	<table><tr><td><ul style="list-style-type: none">• HTN + HF : Diuretics > ACE Inhibitors/ ARBs/ spironolactone</td></tr><tr><td><ul style="list-style-type: none">• HTN + DM : ACE/ ARBs best choice.• Prevent the Remodelling changes + Inc GFR& renal perfusion</td></tr><tr><td><ul style="list-style-type: none">• HTN+ Asthma : Avoid Beta blockers.• Use ACE /ARBs /ca blockers /thiazides diuretics</td></tr><tr><td><ul style="list-style-type: none">• HTN Emergency : IV Nitroprusside (also in asthma)</td></tr><tr><td><ul style="list-style-type: none">• HTN In Pregnancy : Labetalol > Methyldopa</td></tr><tr><td><ul style="list-style-type: none">• HTN emergency in Pregnancy: IV HYDRALAZINE</td></tr></table>	<ul style="list-style-type: none">• HTN + HF : Diuretics > ACE Inhibitors/ ARBs/ spironolactone	<ul style="list-style-type: none">• HTN + DM : ACE/ ARBs best choice.• Prevent the Remodelling changes + Inc GFR& renal perfusion	<ul style="list-style-type: none">• HTN+ Asthma : Avoid Beta blockers.• Use ACE /ARBs /ca blockers /thiazides diuretics	<ul style="list-style-type: none">• HTN Emergency : IV Nitroprusside (also in asthma)	<ul style="list-style-type: none">• HTN In Pregnancy : Labetalol > Methyldopa	<ul style="list-style-type: none">• HTN emergency in Pregnancy: IV HYDRALAZINE
<ul style="list-style-type: none">• HTN + HF : Diuretics > ACE Inhibitors/ ARBs/ spironolactone							
<ul style="list-style-type: none">• HTN + DM : ACE/ ARBs best choice.• Prevent the Remodelling changes + Inc GFR& renal perfusion							
<ul style="list-style-type: none">• HTN+ Asthma : Avoid Beta blockers.• Use ACE /ARBs /ca blockers /thiazides diuretics							
<ul style="list-style-type: none">• HTN Emergency : IV Nitroprusside (also in asthma)							
<ul style="list-style-type: none">• HTN In Pregnancy : Labetalol > Methyldopa							
<ul style="list-style-type: none">• HTN emergency in Pregnancy: IV HYDRALAZINE							

ANTI HYPERTENSION DRUGS	
ACE inhibitor & ARBs	<ul style="list-style-type: none"> ○ Captopril, enalapril etc. Avoid in Pregnancy Renal artery stenosis. ○ Reduce both Preload & afterload. ○ ARBs : Losartan, Valsartan. cause Less cough and toxicity ○ Common side effect : Cough (due to raised bradykinin) angioedema + Hyperkalaemia + Renal toxicity + CKD Avoid in Pregnancy as they cause Renal malformations.
Beta Blockers	<ul style="list-style-type: none"> ○ Propranolol, esmolol, labetalol ○ Cardioselective : Betaxolol, atenolol, Acebutolol ○ Nebivolol : inc Vasodilation and dec LDL. Esmolol is shortest acting. ○ Timolol used in glaucoma. BB are USED IN HTN. HF , Angina , Haemangioma , glaucoma, pheochromocytoma (but always use Alpha blocker before beta blocker in it) ○ S/E : Bronchospasm (avoid in Asthma) Hypotension , dec HR. ○ Avoid in Acute and Decompensated HF. Use in chronic stable HF
Ca Channel blockers	<ul style="list-style-type: none"> ○ Amlodipine , Verapamil , Nimodipine and diltiazem ○ Block L - Type channels : used in HTN. ○ Block T - type channels : used for CNS diseases. ○ Verapamil stops the heart and used In SVT Prophylaxis. it is Cardiac depressant. ○ Nimodipine is used for Sub arachnoid haemorrhage ○ Uses of Ca channel blockers : HTN , Angina , HF , migraine , pre-term labour. ○ S/ E : Dihydropyridines (amlodipine) causes Gingival hyperplasia. ○ Other S/E : Hypotension , Peripheral Edema. Constipation is common
Nitrates	<ul style="list-style-type: none"> ○ dec Pre-Load more due to Venodilation. ○ S/ E : HOT (Headache , Orthostatic hypotension, and Tachycardia ○ Monday Disease: Development of Tolerance for side effects(headache) during working days of week and loss of Tolerance during Weekend and re appearance of symptoms during 1st day (Monday)
Minoxidil Hydralazine Nitroprusside	<ul style="list-style-type: none"> ○ Reduce Afterload by arterial dilatation. ○ Minoxidil is used in Hair fall treatments. ○ Hydralazine for HTN emergency in pregnancy ○ Hydralazine can cause SLE (BCQ) ○ Drugs causing SLE : Procainamide > Hydralazine > Quinidine. ○ Nitroprusside : inc Nitric Oxide synthesis. Used in HTN emergency. ○ Causes Vasodilation of both arterioles and veins
Methyl Dopa & Clonidine	<ul style="list-style-type: none"> ○ both are Alpha 2 agonists. Act on CNS to dec sympathetic flow. ○ Alpha 2 receptor are inhibitory in nature. ○ Clonidine can be used in Diabetic diarrhea. ○ Methyl Dopa may be used in HTN in pregnancy. ○ Methyl Dopa causes Hemolytic Anaemia (Coomb's +ve) ○ Side effect : Sedation & Hypotension

Pre-Eclampsia	Eclampsia	HELLP Syndrome
<ul style="list-style-type: none"> HTN + Proteinuria (> 300 mg/24hrs) after 20 wks. <p>Risk factors :</p> <ul style="list-style-type: none"> Nulliparity Chronic HTN DM, CKD, SLE <p>Pathogenesis:</p> <ul style="list-style-type: none"> Remodelling of vessels (spiral arteries) occurs Alteration in Levels of PGE1 and Endothelin is responsible 	<ul style="list-style-type: none"> Convulsive (seizure) form of Pre-Eclampsia Managed by IV MgSO4 <p>Complications</p> <ul style="list-style-type: none"> HELLP syndrome Cerebral haemorrhage Renal and hepatic failure abruptio placenta maternal mortality and morbidity. <p>For Foetus :</p> <ul style="list-style-type: none"> Premature birth Growth retardation. 	<ul style="list-style-type: none"> Hemolysis Elevated Liver enzymes Low PLT Schistocytes on peripheral smear

ANTI ARRHYTHMIC DRUGS		
5 Classes → Mnemonics: No Bad Boy Keeps Clean		
<ol style="list-style-type: none"> NO: Sodium channel blockers are Class 1 (1A,1B,1C) Order of Na channel blockade: 1C (highest) > 1A > 1B (Weak) BAD BOY: Beta blockers class 2 Keeps: K channel blockers are Class 3 Clean: Ca blockers are Class 4 Miscellaneous: Adenosine and MgSo4 		
AP DURATION	Inc PR	Inc QT
1A inc AP in ventricles) ,1C (AV node) Class IV inc AP	Class II and IV	Class III & Class IA

Class I	<p>CLASS 1A : Quinidine, Procainamide, Disopyramide</p> <ul style="list-style-type: none"> ❖ Used in Ectopic SVTs, both Atria + Ventricular reentrant Tachyarrhythmia. <p>Class 1B: Lidocaine, Mexiletine and Phenytoin.</p> <ul style="list-style-type: none"> ❖ Lidocaine is Doc for post MI ventricular Arrhythmias -- BCQ <p>Class 1C: Flecainide and propafenone. never give Post MI or in structural heart diseases. Used in SVTs i.e A Fib. last resort in refractory VT</p>
Class III	<ul style="list-style-type: none"> ❖ Amiodarone Is broad spectrum drug having Class I-IV effects. ❖ Amiodarone may cause Hypothyroidism > Hyperthyroidism, Metallic taste, and Pulmonary fibrosis. ❖ Sotalol, ibutilide, dofetilide may cause torsade's de Pointes.
Class IV	<ul style="list-style-type: none"> ❖ Diltiazim and Verapamil (prophylaxis of SVT)
Class V	<ul style="list-style-type: none"> ❖ Miscellaneous: Adenosine -- DOC for SVT .it inc K+ efflux. ❖ Magnesium is effective in Torsade's de Pointus and digoxin toxicity

Ivabradine:

- ❖ prolongs phase IV depolarization by blocking funny sodium channels.
- ❖ Used in LHF & HFrEF & chronic stable angina.

PAST PAPERS BCQs – ONE LINERS

1. IHD / CAD are MCC of Sudden cardiac death overall. SCD occurs without symptoms or < 1hr after symptoms arise.
2. Most common aetiology of SCD is acute ischemia in 90 % cases.
3. Central Chest Pain for 3hrs which enzyme is raised = CKMB
4. Chest pain and sweating for 4hrs which marker is raised = CKMB , after 4 hrs = Trop T
5. Confirmatory marker for MI = Trop I – Gold standard as well
6. Cyanotic spell while running or playing game in child = TOF
7. Heart diseases involve which valve mostly = Mitral valve
8. Pansystolic murmur at left sternal border on ECHO. VSD is seen , defect lies in = Membranous part of IVS
9. Patient died 4 hrs after MI the likely cause is = Arrhythmia (V Fib). 4 – 24 post MI death = Arrhythmia
10. ST elevation on leads II , III , avF which wall is involved = Inferior wall M
11. The vessel involved in inferior wall MI is = RCA
12. Patient died of hypertension , on autopsy vessel lacked tunica media which type of aneurysm = Berry aneurysm
13. In above Scenario , cause of death = Dissection but type of aneurysm is berry aneurysm
14. LCX blockade seen on angiography the finding = Circumferential infarct of posterior/posterolateral wall of Lt ventricle
15. A 25 yr. male presented with unequal BP in both arms ,visible intercostal pulsation, and rib notching on CXR the diagnosis is = Post ductal Coarctation of aorta
16. QRS complex shows = Ventricular depolarization and ST segment shows = Complete Vent Repolarization.
17. QT interval represents = Entire systolic phase
18. AV nodal delay results in = Prolonged PR interval (Not Segment)
19. Aortic root dilatation + lens dislocation the cause is = Inherited defect of Fibrillin – 1 (Marfan syndrome)
20. Sudden chest pain + hemoptysis one week after delivery , no fever ECG shows S1Q3T3 pattern the appropriate investigation = CT Angiogram or Gallium scan (diagnosis = Pulmonary embolism)
21. A patient on Beta blocker presented with prolonged PR interval the cause = Drug induced 1 st degree heart block (beta blockers)
22. 2 nd degree heart block results in = Atrial rate > Ventricular rate
23. Systolic phase of cardiac cycle corresponds to = QT/RT interval
24. Pansystolic murmur at aortic area with long standing pulse and left axis deviation = MR > TR
25. Most specific finding in AR = Early diastolic murmur > Bounding pulse
26. Fever for 2 wks. + Chest Pain radiating to back with right parasternal rustling on auscultation = Pericarditis
27. Pain relates to respiration = Pericarditis (pain relieves on sitting forward). Pain unrelated to respiration = Myocarditis
28. Retrosternal chest pain , sweating and dyspnea with BP 90/60 and low vol pulse 105/m the likely diagnosis = MI
29. A shopkeeper died after sudden chest pain that resulted into collapse . The cause = Pulmonary Embolism (sudden chest pain with sudden collapse is PE)
30. Most specific finding on ECG in PE = Sinus Tachycardia , NOT S1Q3T3 (rarely seen)
31. Loud S1 is seen in = Mitral stenosis. Loud S1 on auscultation the finding may be = PR interval lower limit
32. Commotio cordis/Cardiac Concussion is Sudden death related to v fib during sports injury. E.g during baseball/ playing hockey leading to chest wall trauma
33. Common cause of sub-acute endocarditis = S.Viridians
34. Patient came in ER with failing heart DOC is = Dopamine > Dobutamine. The DOC in cardiac arrest = Adrenaline
35. Headache + jaw claudication in a 65yr old female. On Biopsy temporal artery is firm = Giant cell arteritis
36. For CVP right atrium level taken at = Manubriosternal angle > 4 th ICS
37. Common cyanotic heart disease = TOF
38. In Mitral stenosis which is absent on JVP = A wave
39. Irregularly irregular pulse and irregular R – R Interval = A Fib

40. A Fib on ECG shows = Irregular R – R interval → specific finding in A Fib
41. 72 yr old man collapsed. ECG shows atrial rate 75bpm and Vent rate 35 bpm the cause = Stokes Adam syndrome (3 rd degree block with syncope)
42. Finding specific for acute MI = ST Displacement. Earliest changes in MI = T wave changes (Tall in STEMI)
43. Pulse pressure is increased in = HTN
44. 42 yr old man with H/o slowly developing CCF . His BP, angiography , TLC and ESR is normal. The diagnosis = Cardiomyopathy (Congestive or Dilated type)
45. 4 days post MI patient is at danger of = Myocardial rupture → Cardiac tamponade
46. CVS Change in Old age/Geriatric = Systolic HTN
47. A 10 yr old girl diagnosed with acute rheumatic fever dies instead of recovering. The likely cause = Myocarditis
48. Chest pain while climbing stairs or jogging = Stable Angina pectoris
49. 85 yr old woman dies due to Colon cancer. On autopsy, small fibrin deposits seen around line of closure of mitral leaflets. The valvular lesions represent = Marantic or Non – bacterial thrombotic endocarditis
50. Central line is indicated in = For Hyper elimination
51. A 12 yr old boy presented with recurrent epistaxis with +ve family history for it. The most likely condition = Osler Weber – Rendu syndrome
52. Typical lesion of hereditary hemorrhagic telangiectasia is on = Lips
53. Feature of A fib = Irregular R – R Interval > P wave absent. Remember that it is R – R Interval, not segment here.
54. On inspiration = JVP and BP fall but Heart rate increases and S2 splits
55. In Patients with Urinary Catheters, GI or Genitourinary procedures the cause of endocarditis = Enterococci → Streptococcus Faecium and S. faecalis
56. Low voltage ECG is a feature of = Old MI or Recurrent MI
57. Most common defect in ASD = Ostium secundum defect. If patency of PDA is required, give = PGE1
58. Fixed splitting of S2 in = ASD. Major risk factor for development of atherosclerosis = Hypercholesterolemia
59. Polycystic kidney disease is associated with = Berry Aneurysm
60. Tearing chest Pain in a HTN male radiating to back with Widened mediastinum = Aortic Dissection
61. Multiple purple skin lesion on arms and legs seen in AIDS patient = Kaposi Sarcoma → HHV – 8
62. Polyarteritis Nodosa is linked to = HBV in 30% cases
63. 15 yrs old Lady presents with fever , malaise , arthritis , cold upper extremities and weak radial pulses. On MRI 70% stenosis of main arteries arising from aorta = Takayasu arteritis
64. 4 yr old child with Cervical lymphadenopathy + Edema of hands and feet + Conjunctival erythema. He is at risk of developing which life-threatening complication = Coronary Aneurysm (Kawasaki disease)
65. 30 yr old male having BP 250/140 mmHg dies despite of all measures and medications. At autopsy which will be the finding = Multiple punctate hemorrhages in kidneys – flea bitten kidneys
66. 34 yr old female presented with elevated BP despite of medications. The physician thinks of secondary HTN. What is a well-known cause of 2 nd ry HTN = Renal artery stenosis
67. A 20-month-old boy with tuberous sclerosis dies suddenly. At autopsy heart was normal except two yellow masses consisting of large cells with clear cytoplasm. Which mutation is associated with it = Hemartin + Tuberin
68. A 29 yr male presented with Painful , solitary 1 - 2 cm reddish blue nodule surrounding nail bed. On histology sheets of uniform cells around small blood vessels seen = Glomus tumor
69. A 50 yr male having squeezing chest pain presented to ER. Troponin I was raised on testing. If he dies today what findings can be there = Coagulative necrosis + Neutrophil infiltration
70. A 9 yr old boy presented with h/o sore throat 2 week ago that is recovering without antibiotics. O/E friction rub and new heart murmur with Migratory polyarthritis and raised ASO titres. The most likely outcome in this patient = Total recovery after 1 – 2 months with no complications or sequelae
71. Though Mitral valve disorders occur in chronic stage in ARF but most likely and common outcome is Recovery

72. A 49 yr old male with angina , +ve syphilis tests (RPR , VDRL and FTA – ABS).On ECHO what will be findings = Aortic valve insufficiency + linear calcifications along ascending aorta
73. A 60 yr old male having weakness in left leg , MRI brain reveals small ischemic infarct. Angiography and ECHO reveal normal arteries and valves with no vegetation but a small right to left shunt. The condition of patient associated with symptoms = Atrial septal defect (Paradoxical embolism)
74. A 70 yr old lady having dyspnea , Orthopnea , PND and syncope. She is diagnosed with primary heart tumor causing ball valve obstruction = Myxoma (more common in left atrium)
75. Right sided HF is linked to = Diseases of Lungs or Pulmonary vessels
76. A 15 yr old tall thin girl with long slender fingers presents with Palpitations. O/E Midsystolic click is found. The cause of murmur is = Mitral valve prolapse (diagnosis is Marfan Syndrome)
77. Mitral valve prolapse is associated with = Myxoid degeneration
78. Severity of MS correlates with = Duration of murmur
79. Smoking is a risk factor for = Buerger's disease. Typical Pt is 35 yr old male smoker.
80. After an episode of flu like illness a patient presented to ER with chest pain and dyspnea. ECG is abnormal, large Pericardial effusion present. ANA is -ve. The patient tends to collapse and Pericardiocentesis performed to drain fluid. The fluid in clear straw color with few inflammatory cells. Most likely etiology = Viral infection
81. Patient presented with chest pain. What is your 1 st Question = Tell me more about the pain
82. Atheroma is Common in = Males. Strep viridians is not commensal on Skin
83. Mitral stenosis murmur = Apex. McCallum Patch Present in rheumatic fever (LA)
84. Not occurs in Rheumatic fever = Rupture of chordae tendinae
85. Aortic and Mitral involvement = Libmann sac endocarditis
86. Severity of Mitral stenosis = Length of diastolic murmur
87. Most common congenital heart disease = VSD
88. When the Cardiac tissue is most vulnerable to Ventricular fibrillation – Just at the end of AP
89. 1 st Heart sound is VARIABLE in A Fib. Blood flow to tissues maintained by MAP
90. Baroreceptors are present in adventitia of large arteries
91. Hypoglycemia causes increased QT interval. Neurogenic shock causes decreased TPR
92. Most common source of systemic emboli = Left Ventricular Mural Thrombus
93. Cardiac tamponade feature = Pulsus paradoxus. Coronary Blood flow increased by = Adenosine
94. What decreases Blood supply to brain = Seizures
95. Upper and lower limit of cerebral Blood flow autoregulation = 50-150
96. Increased SV due to large blood VOLUME
97. During inspiration JVP drops due to increased venous return
98. Most common cause of Hypertension = idiopathic
99. Normal Mitral valve area = 4-6 cm ²
100. Extend to Right atrium = clear cell renal carcinoma
101. Pericarditis = PR depression > Widespread ST elevation > ST depression
102. HOCM = Midsystolic murmur reduced by Valsalva and isometric handgrip
103. Dilated cardiomyopathy = Mitral and tricuspid regurgitation
104. Temporal giant cell arteritis DOESNOT WORSEN ON EXPOSURE TO HEAT
105. Sturge Weber syndrome is related to = Glaucoma
106. Lesions that Do not regress = Port wine stain
107. Strawberry Hemangioma regress spontaneously by 5 years
108. Cyanosed toes after exposure to cold = Raynaud's phenomena
109. Smoking may cause = thromboangitis obliterans (another name on Buerger disease)

110. Time interval b/w 1 st and 2 nd heart sound = ventricular systole
111. Shock WITHOUT Vasodilation associated with = BURNS
112. In exercise venous blood returns to heart by = Muscle pump in Calves
113. Circulation in heart maintained by = Local metabolites
114. PAN = Fibrinoid necrosis
115. Parasympathetic stimulation = decreases HR
116. Extent to which tissue gets disturbed by occlusion of its blood supply Depends on = Rate of development of Thrombosis
117. Venous pressure increases 8mm, effect on capillary pressure = NO
118. Vagus decreases HR by Potassium conductance
119. Blood Pumped by heart = 5 Liters/minute
120. Splitting of S-2 = Delayed closure of Pulmonary valve
121. Infarction In V1-V4 = Anterior infarction STEMI
122. Supply Of Interventricular septum is = Anterior inter ventricular Artery
123. Resuscitation of hypovolemic shock = Increase in urine output Successful
124. Initiation of electrical activity of heart = SA node
125. U-wave = papillary muscle depolarization
126. Low voltage QRS complex = Old MI
127. Patient with LVH, increased Left Atrial Wedge pressure and diastolic Murmur = Aortic regurgitation
128. What determines TPR index = Diastolic pressure
129. Fastest conduction in Purkinje = Largest diameter
130. Max systolic BP in = renal arteries
131. Maximum feedback gain = Baroreceptors
132. Saw tooth waves = Atrial flutter
133. HR b/w 200 and 350/minute = Atrial flutter
134. HR of 40/minute seen in = 3 rd degree heart block/Complete heart block
135. In Atrial fibrillation = Pulsus deficit can be present
136. Common cause of Chronic Constrictive or fibrous pericarditis = Tb
137. Pathogenesis of rheumatic fever = Molecular mimicry
138. Mid diastolic murmur + RVH + LA enlargement is seen in = Mitral stenosis
139. Tall QRS = Hypertrophy of ventricles
140. Isoelectric line = PR segment. Isoelectric segment = ST segment
141. Time taken by impulse to reach from endocardium to Epicardium = QRS complex
142. From Epicardium to Endocardium = QT interval
143. PR segment on ECG coincides with = A wave on JVP
144. No ECG changes seen in = Sleep → also Cardiac output remains unchanged in sleep
145. Hypokalemia = U wave > inverted T wave. Hyperkalemia = Tall T wave
146. Common congenital cyanotic anomaly at birth = TGA
147. Hamartomatous growth in Rt Ventricle in a 5yr old child = Rhabdomyosarcoma (Not Angiosarcoma)
148. A pt dies suddenly, cocaine is detected in blood. What will be finding = Contractile band necrosis
149. Non-bacterial thrombotic endocarditis NBTE is linked to = Terminal Neoplasms
150. Valves common involved in Libman Sacks endocarditis = Mitral and aortic
151. Child with machinery like murmur = PDA (Prematurity is common risk factor for PDA)
152. Left Vent failure is caused by = Aortic valvular disease
153. Imp clinical feature of water intoxication = Slow Pulse (Bradycardia)

154. PaCO ₂ is 100% in = Left to Right shunt
155. 80 yr old man with symptoms of LVF and pulmonary edema. On X-ray cardiomegaly seen. A cause of HF is = Bicuspid calcific aortic valve
156. MS murmur best heard at = Apex
157. On Auscultation at Left 3 rd ICS which area is = Aortic 2 (A2). Mitral area = Left 5 th ICS at MCL
158. Best diagnostic or Confirmatory for Rheumatic fever = Throat culture > Blood culture
159. Initial test for ARF = ASO titres
160. Cystic mass in Left parietal lobe with heart involvement = Myxoma
161. In Complete heart block = Ventricle rate doesn't correspond to atrial rate
162. In Coarctation of aorta = Constriction just after Subclavian artery origin
163. 56 yr old lady has non lethal MI. What is the risk after few minutes = Arrhythmia
164. After tonsillectomy a pt becomes hypotensive due to = Blood loss (Hypovolemic shock)
165. A pt died due to a vessel occlusion in brain after episode of A fib. The cause = Embolism
166. Young HTN female dies of Hemorrhagic stroke. On Autopsy petechiae on kidneys with hyperplastic arteriosclerosis and Fibrinoid necrosis. The diagnosis = Fibromuscular dysplasia - a case of 2° HTN with RAS.
167. C – ANCA + ve in = Wagner granulomatosis (Vasculitis)
168. Large friable irregular vegetations = infective endocarditis
169. Gold standard test for IE = Blood culture. MCC of acute endocarditis = Staph Aureus
170. PDA characteristic feature = Peripheral cyanosis > Inc arterial PCO ₂ .
171. Heart failure may be seen in = Fibrinous pericarditis
172. H/o CKD in a patient presented with deranged RFTs and Rustling sound on chest Auscultation. The cause is = Uremic pericarditis (A type of Fibrinous Pericarditis)
173. Initial L to R shift before reversal seen in = Eisenmenger syndrome
174. Post MI death on 4 th day. On Biopsy finding may be = Neutrophils, macrophages, necrosis
175. Obese Shopkeeper with sedentary life style presented with raised BP. All investigations came out to be normal. His raised BP is due to = Increase vascular tone (as Vasoconstriction inc TPR + BP)
176. Sodium retention is seen in = Heart failure
177. Feature of Hypovolemic shock = Venous and venules constriction (systemic Vasoconstriction)
178. Unifascicular block feature is = Left axis deviation
179. Bifascicular block = Prolonged PR interval + (Lt Anterior fascicular block/RAD)
180. Trifascicular block = Prolonged PR + LAD
181. S1 is variable in = A fib
182. MS + Loud S1 + Pulmonary HTN and dyspnea. What can be other finding = RVH
183. In Neurogenic shock = Loss of Vasomotor tone (dec TPR)
184. Neutrophils in necrotic area post MI seen after = 24 hrs
185. AR murmur may be auscultated at = Right 2 nd ICS (A1)
186. Heart failure may result in = Pericardial effusion (Transudate type)
187. Diagnostic test for giant cell arteritis = Biopsy
188. Absent tunica media in which type of aneurysm = Berry aneurysm
189. Type A personality people are at risk of = Cardiovascular disease
190. Type A personality vulnerable to IHD due to = Physiological stress and competitive nature
191. Severe HTN 180/110 in a 50 yr male. He is at risk of = Hyperplastic arteriosclerosis
192. Known case of IHD with chest pain. On exam Diastolic murmur with low preload due to = MS
193. Finding in Cardiac tamponade = Pulsus Paradoxus (remember BECK'S triad also)

194.S1 Loud + Mid diastolic murmur + Opening snap + Tapping apex beat = Mitral stenosis (MS)
195.Prolong QRS complex in Lead II indicates = Ventricular hypertrophy
196.Aortic insufficiency may be a finding in = Ankylosing spondylitis
197.AV septum is ruptured. Which valve is affected = Tricuspid
198.Collapsing pulse + diastolic murmur = Aortic regurgitation
199.Murmur of AS may radiate to = Neck
200.Chest pain, normal Cardiac enzymes but Intercostal tenderness = Costochondritis
201.HTN retinopathy involves changes in = arterioles (narrowing)
202.A pt presented with weight loss, palpitations ,enlarged thyroid gland, Sinus rhythm on ECG. The problem can be = Paroxysmal atrial fibrillation (due to Hyperthyroidism)
203.Abdominal Pain + palpable purpura on buttocks = Henoch schlein purpura
204.Heart sinking + low amplitude T waves = Hypokalemia
205.Difference between anaphylactic and hypovolemic shock = Increase Cardiac Output
206.Septic shock differs from Hypovolemic by = CO
207.A pt came with new murmur and H/O Rheumatic fever in childhood. The cause = MS
208.Male with Chest pain for 30 mins.O2 and S/L Angised given. Next step is = Enzyme levels
209.In Essential HTN what is increased = Increase Workload
210.Cause of edema in CCF = Inc Hydrostatic pressure
211.Fever + murmur + Splenomegaly. The treatment is = Inj Penicillin + Gentamycin (case of IE)
212.Inflammatory marker related to IHD = CRP
213.Diabetic smoker and HTN patient is at risk of = Atherosclerosis > Atheroma
214.An alcoholic patient with raised JVP and Nutmeg liver (chronic passive hepatic congestion).The cause = Chronic alcoholism. If diagnosis/disease/condition is asked, then it is RHF/CCF
215.HTN male having severe chest pain radiating to back dies. On autopsy finding is = Medial Necrosis (A scenario of Aortic dissection – medial necrosis or cystic medial degeneration is a feature)
216.Artery involved in Posterior wall MI = RCA
217.Infarct of posterior septum will cause injury to = AV node
218.In anaphylactic shock = arteriolar dilatation + Venous dilatation occurs
219.First to rise in acute MI = Myoglobin
220.Omphalocele is associated with = VSD
221.A patient dies of pneumoniae. The finding can be = Inc Vascular permeability (sepsis)
222.Old man with HF + Pleural effusion. In Pleural tap finding will be = Heart failure cells
223.A soldier taken to Siachen at 15000 ft. height develops dyspnea after 10 hrs due to = Pulmonary edema (HAPE and HACE are lethal complications)
224.MCC of thoracic aortic dissection in HTN patient = Medial degeneration
225.Lesion of different ages seen on biopsy in a vessel in = PAN
226.IE occurs commonly in = IV drug abusers – IVDA
227.6 yrs. old child with H/o Aortic aneurysm and chest pain due to = Kawasaki disease
228.Newborn having dyspnea , SOB and Blue discoloration due to = TGA
229.1 Lit blood loss in 5 min. What will occur = Decrease TPR
230.After 1.5 L blood loss what will occur = Low BP
231.A pt in cardiac diastole having backflow of blood which is heard as murmur. The murmur is = Early diastolic murmur (AR)
232.2 P waves followed by QRS due to = Dec AV nodal conduction
233.Moderate hemorrhage can be clinically diagnosed by = Postural dizziness

234. Fatty Plaque composition = Lipids + Smooth muscles , cells + ECM
235. Neuroendocrine response after surgery = Hemorrhage
236. Characteristic feature of rheumatic fever related to valves = Mitral stenosis
237. After RTA a pt with BP 90/50 , tachycardia, and low urine output. Renin was increased due to = Decrease in arterial blood flow (not BP , it is dec blood flow here)
238. Chronic pressure overload in LV due to AS results in = LVH
239. Most common site of atherosclerosis = Abdominal aorta – infra renal part
240. Post MI what type of shock may happen = Cardiogenic shock
241. Biochemical changes post MI = Anaerobic glycolysis
242. Cause of ARF = Group A Beta hemolytic streptococcus
243. During normal systole backward blood flow to heart seen as = Dicrotic notch
244. RV containing Hemorrhagic and necrotic area = Rhabdomyosarcoma
245. In Compensatory shock finding = Metabolic acidosis + Resp alkalosis or it can be asked like :
246. : Pt in shock reversed phenomena operating will be = Met Acidosis + Resp Alk
247. Approach to Pericardiocentesis = Subxiphoid best > 5 th Left ICS close to sternum
248. Post MI on Angiography LCA blocked. After 03 days what will be abundant in that infarcted area = VEGF (Granulation tissue formation starts on 3 rd day in healing)
249. Which type of Fats linked to IHD/CAD = TRANS Fatty acids (Unsaturated fats are protective)
250. Sustained inc CO occurs in = Anemia
251. Old male with H/o IHD presented with irregular pulse and abnormal QRS. DOC = Lidocaine
252. Pt having IHD develops chest pain due to = coronary artery disease (CAD) > Thrombus
253. The underlying mechanism for chest pain in IHD = Thrombus
254. Aschoff body degeneration, initial stage = Fibrinoid degeneration
255. ST depression in V2 V3 and R wave = Posterior wall MI
256. Actually, On ECG Post wall MI shows = Tall R wave in V1,V2 and ST depression in V1 – v4
257. Origin of myxoma = Fossa Ovalis (LA)
258. Myocyte disarray seen in = HOCM. 1 st line drug and DOC in HCOM = Beta blockers
259. A pt on Potassium sparing diuretics , ECG will show = Tall T Waves (Hyperkalemia)
260. Most common sequelae of RHD = mitral stenosis
261. MI of posterolateral heart vessel involved = LCX. Infarct of LA + LV vessel responsible = LCX
262. Progressive Prolongation of PR with dropped beat = Mobitz 1 AV block
263. Prolonged PR without another finding = first degree heart block
264. A female on prolonged immobilization has Complained of SOB and dyspnea/E Peripheral edema + Nutmeg liver found. CXR shows areas of infarction. The cause is = Recurrent Pulmonary embolism (History of Immobilization/bed rest → DVT → PE (recurrent – many infarcts here)
265. Common feature of Pulmonary embolism = Clinically silent. A child with cyanosis + inc A – a gradient = TOF
266. Ventricular septal wall thicker than ventricle wall seen in = HCOM
267. Emboli first go to = IVC > Rt Atrium. Emboli 1 st lodge in = Pulmonary artery branches
268. In dilated cardiomyopathy what happens = Systolic dysfunction. Commonest congenital heart disease = VSD
269. Giant cell arteritis is linked to = Polymyalgia Rheumatica
270. Lesion of same ages seen in which vasculitis = Microscopic Polyangiitis
271. Re - entry circuit occur due to = Paroxysmal nodal tachycardia
272. In shock Aerobic to anaerobic metabolism occurs due to = imbalance of O2 supply & demand

273. Long standing pulmonary congestion in MS leading to HF The cells lining alveoli on autopsy will be = Heart failure cells (Hemosiderin laden macrophages)
274. Systemic arterial emboli mostly arises from = Left Ventricle – mural thrombus in 80% cases.
275. Hypertension affects arterioles more and DM affects Capillaries
276. 1P wave followed by 2 QRS pacemaker lies in = AV node
277. 2P waves followed by 1 QRS here pacemaker lies in = SA node. Pacemaker is required due to defect in = SA node
278. Pacemaker required due to defect in conduction of = AV node
279. Moderator band present in = RV. In Complete Heart block pacemaker is placed at = Rt Ventricle
280. Normal ECG can't record activity of = SA node. Hemopericardium can occur in = Scurvy
281. Which type of myosin present in heart = Alpha + beta. In HOCM defect lies in = Beta myosin heavy chain
282. Treatment of Vasospastic or Prinzmetal angina = Ca ⁺ channel blockers. Give nitrates in acute or emergency cases
283. Digoxin does not cause which block = Mobitz – II Block

Most common Overall CHD → VSD, also MC in Child → VSD. While MC CHD in Adults : ASD
MC Large Vessel disease: PDA (Hilly areas + Congenital Rubella syndrome)
MC Cyanotic disease overall: TOF .MC cyanotic present at birth: TGAs
Boot shaped Heart seen in TOF due to RVH. Egg on string shaped Heart in TGA
Shunt is necessary for survival in : TGA. Infant of Diabetic Mother : TGA
Lithium is a known cause of Ebstein anomaly. Alcohol exposure → VSD > PDA , ASD and TOF
ECHO > ECG is diagnostic for CHD
Down syndrome MCC of Endocardial cushion defect
In Turner syndrome: Bicuspid valve > Pre ductal Coarctation of aorta

RESPIRATORY SYSTEM

LUNG VOLUMES (Mnemonics = LITER)	
Tidal Volume	<ul style="list-style-type: none"> The volume inspired or expired with each normal breath (Or) Air that moves into lung with each quiet inspiration is V_T. $V_T = 500 \text{ mL}$
Inspiratory reserve volume (IRV)	<ul style="list-style-type: none"> The volume that can be inspired over and above the tidal volume. It is used during exercise. It is the air that can still be breathed in after normal inspiration. $IRV = 3000 - 3300 \text{ mL}$
Expiratory reserve volume (ERV)	<ul style="list-style-type: none"> The volume that can be expired after the expiration of a tidal volume or we can say it is air that can still be breather out after normal expiration. $ERV = 1000 \text{ mL}$
Residual volume (RV)	<ul style="list-style-type: none"> The volume that remains in the lungs after maximal expiration. Any Lung capacity that involves RV cannot be measured by spirometry. $RV = 1200 \text{ mL}$
LUNG CAPACITIES	
Lung Capacities are sum of two or more Lung volumes. RV, TLC & FRC can't be measured by spirometry. Vital capacity doesn't include RV.	
Inspiratory Capacity	<ul style="list-style-type: none"> Sum of $TV + IRV$. $IC = 3800 \text{ ml}$.
Functional Residual Capacity (FRC)	<ul style="list-style-type: none"> Sum of $ERV + RV$ (BCQ). $FRC = 2200 \text{ ml}$ It is the volume remaining in lungs after expiration of V_T. As it includes RV, so, can't be measured by spirometry
Forced Vital Capacity or Vital Capacity (FVC / VC)	<ul style="list-style-type: none"> It is sum of : $TV + ERV + IRV = 4800 \text{ ml}$ The volume of air that can be forcibly expired after maximal inspiration
Total Lung Capacity (TLC)	<ul style="list-style-type: none"> Sum of all 4 volumes. $TLC = 5800-6000 \text{ ml}$ It is the vol in lungs after a maximal inspiration. It also includes RV so cannot be measured using spirometry.

LUNG VOLUME AND CAPACITY

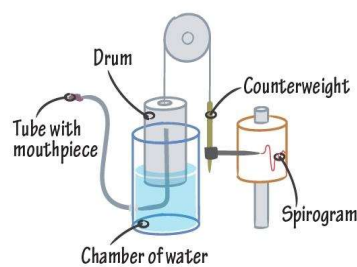
Spirometer
Measures pulmonary function

Key Values

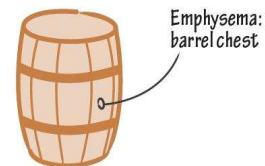
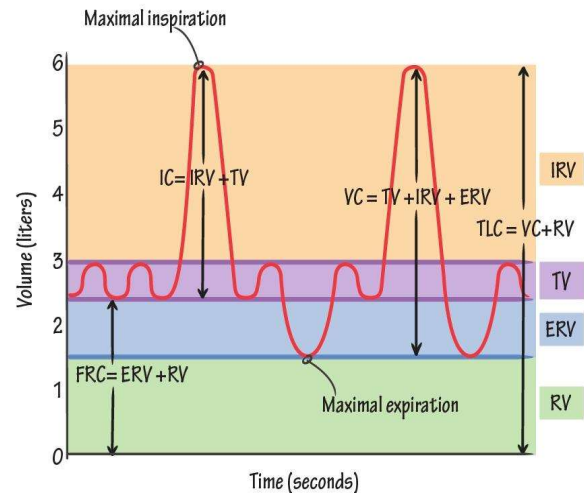
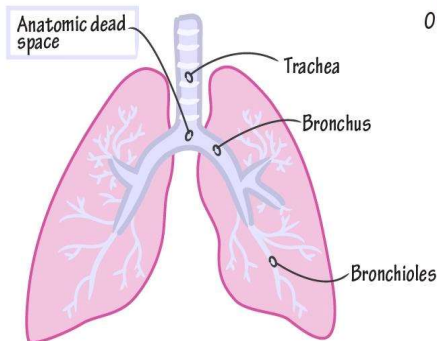
- ✓ Tidal volume: air inspired during quiet breathing
- ✓ Inspiratory reserve volume: extra volume of air that can be inspired after standard quiet breath
- ✓ Expiratory reserve volume: extra volume of air that can be exhaled after standard quiet breath
- ✓ Residual volume: air in lungs after maximal expiration

Lung Capacity
Sum of 2 or more lung volumes

- ✓ Vital capacity
- ✓ Total lung capacity
- ✓ Inspiratory capacity
- ✓ Functional residual capacity



- ✓ Healthy lungs: Physiologic dead space = anatomic dead space
- ✓ Emphysema: Physiologic dead space > anatomic dead space
Residual volume increases



Forced Expiratory Volume (FEV1)

- It is the volume of air that can be expired in the **first second** of a forced maximal Expiration.
- FEV, is normally 80% of the forced vital capacity, which is expressed as:

$$FEV1/ FVC = 0.8 \text{ or } 80 \% \text{ (Normal)}$$
- In obstructive lung disease**, such as asthma and chronic obstructive pulmonary disease (COPD), both FEV1 and FVC are reduced, but FEV1 is reduced more than FVC is -- thus **FEV1/FVC is decreased**.
- In restrictive lung disease**, such as fibrosis, both FEV 1 and FVC are reduced, but FEV1 is Reduced less than FVC is thus, **FEV1/FVC is increased or may remain same**

DEAD SPACE

Anatomical Dead Space	<ul style="list-style-type: none"> It is the volume of the conducting airways from Nose to terminal bronchioles. It doesn't take part in gas exchange. It is normally 150 mL approx. So, Conducting Zone = Anatomical dead space Function of conducting zone is humidification , warming and moisturizing. 	
Physiological Dead Space	<ul style="list-style-type: none"> It is defined as the volume of the lungs that does not participate in gas exchange (functional measurement) It is approximately equal to the anatomic dead space in normal lungs. May be greater than the anatomic dead space in lung diseases in which there is Ventilation/perfusion (V/Q) defects. $VD = VT \times PACO2 - PECO2/PACO2$ <ul style="list-style-type: none"> Vd = Physiological dead space , VT = Tidal volume PACO2 → PaCo2 of alveolar gas = PaCo2 arterial blood PECO2 = Paco2 of expired air VD includes anatomical dead space + alveoli which do not take part in gas exchange (alveoli that are poorly perfused or not perfused) In V/Q mismatch → Physiological dead space > Anatomical dead space 	
Factors Affecting Dead Space	Increased Dead Space	Decreased Dead Space
	Hypotension , Standing, neck extension. ETT intubation, Bronchodilation Smoking, Asthma, Emphysema , Bronchitis Pneumonia, Heart failure and Pulmonary Embolism	Hyperventilation, Neck flexion, Supine Tracheostomy , Bronchoconstriction, Atelectasis Sleep Maxillectomy
<p>Pattern of Breathing doesn't affect dead space. Prefer Shallow breathing > Deep breathing for the factor not affecting dead space.</p> <p style="text-align: center;"><u>MNEMONICS</u></p> <p><u>Factors inc dead space :</u> A Hypotensive smoker standing with neck extended and ETT in place as he has Asthma, COPD, Pneumonia, Heart failure and PE.</p> <p><u>Factors decreasing dead space :</u> A jawless sleeping supine hyperventilating with neck flexed having Atelectasis , bronchoconstriction and tracheostomized</p>		
MINUTE VENTILATION		ALVEOLAR VENTILATION
<ul style="list-style-type: none"> The total vol of gas entering in lungs per minute. $VE = VT \times RR/\text{min}$ Normal RR = 12 – 20 Breaths/minute Normal Tidal Volume (VT) = 500 mL/breath If RR = 12/m, VE = 12 × 500 = 6000 mL (6 Lit) 		<ul style="list-style-type: none"> The total vol of gas that reaches/enters alveoli per min. $VA = (VT - VD) \times RR/\text{min}$ Normal VD = 150 mL/breath If RR = 12/min. Then , VA = (500 – 150) × 12 = 4200 mL (or 4.2 Lit)

Ventilation is the Provision of fresh air into lungs. It is the first step of breathing.

MECHANICS OF BREATHING / RESPIRATION

(Exchange of gas between body and external environment)

INSPIRATION		EXPIRATION		
Inhalation or insp is an active process involving movement of air into lung via following events : 1. Thoracic volume increases as the Chest wall and lungs expand. Lung vol increases by one VT (FRC + VT) 2. Rib cage moves forward and outward (also sternum) 3. Diaphragm + External ICM contract and internal ICM relax. Diaphragm becomes flat and moves downward. 4. Pulmonary pressure falls , alveolar pressure decreases than atmospheric pressure leading to expansion of alveoli which cause movement of air inside lungs until the alveolar pressure becomes equal to atmospheric pressure 5. Intrapleural pressure becomes -ve in inspiration → responsible for lymphatic drainage of lung		A passive process in which air containing CO ₂ goes out from lungs through following mechanism : 1. Thoracic volume decreases as the chest wall contracts and lungs are compressed (FRC - VT) 2. Rib cage moves downward and inward 3. Diaphragm relaxes and becomes dome shaped 4. External ICM also relax. Internal ICM contract mainly in forced expiration 5. Alveolar pressure (air pressure in lungs) becomes more than atmospheric pressure leading to expulsion of air outside lungs to environment. • Inspiration takes 1 sec and Exp takes 3 sec in a breathing cycle		
Muscles of inspiration		Muscles of Expiration		
Quite Inspiration	Forceful inspiration	Normal Expiration	Forceful expiration	Accessory muscles
Diaphragm External ICM → both in Quite + forced inspiration	SCM Serratus Anterior Scalenus Anterior Scalenus Medius Pect minor	Passive elastic recoil of lungs plays major role.	Internal ICM > rectus abdominus	Rectus abdominus External oblique

Key Facts

1. **Vertical diameter increased by diaphragm.**
2. Bucket – handle movement of rib cage / ribs elevation increases Transverse diameter.
3. **AP diameter** is increased by **External ICM** mainly with internal ICM & inner most ICM.
4. Pump Handle Movement increases AP diameter -- sternum moves upward + forward.
5. **Most of work of breathing is used in Elastic Recoil of lungs.**

COMPLIANCE OF RESPIRATORY SYSTEM ($C = \Delta V / \Delta P$)

- It is the **change** in Volume for a given change in pressure. $C = \Delta V / \Delta P$. **Mnemonics : CVP**
- It is Analogous to capacitance in CVS.
- It describes **distensibility of lungs & chest** and inversely to stiffness or elastance.
- Compliance of lung – chest wall system (flatter curve) is less than compliance of lungs or chest alone.
- Compliance is the slope of pressure volume curve as explained in diagram given on next page.

Compliance of the Lungs	Compliance of Lung – Chest wall system
<ul style="list-style-type: none"> Transmural pressure is alveolar pressure minus intrapleural pressure (- 5cm H₂O at rest/ FRC) When the pressure outside of the lungs (i.e intrapleural pressure) is negative, the lungs expand and lung volume increases. When the pressure outside of the lungs is positive, the lungs collapse and lung volume decreases. In the air-filled lung, inflation (inspiration) follows a different curve than deflation (expiration); this difference is called hysteresis and is due to the need to overcome surface tension forces at the air-liquid interface when inflating the lungs. In the middle range of pressures, compliance is greatest, and the lungs are most distensible. At high expanding pressures, compliance is lowest, the lungs are least distensible, and the curve flattens. 	<ul style="list-style-type: none"> At rest lung volume is at FRC and the pressure in the airways and lungs is equal to atmospheric pressure = 0 Under these equilibrium conditions, there is a collapsing force on the lungs and a expanding force on the chest wall At FRC, these two forces are equal and opposite. So, the combined lung-chest wall system neither wants to collapse nor wants to expand (i.e equilibrium). As a result of these two opposing forces, intrapleural pressure is negative (sub atmospheric) If air is introduced into the intrapleural space (pneumothorax) , the intrapleural pressure becomes equal to atmospheric pressure. Without the normal negative intrapleural pressure, the lungs will collapse (their natural tendency) and the chest wall will spring outward (its natural tendency).

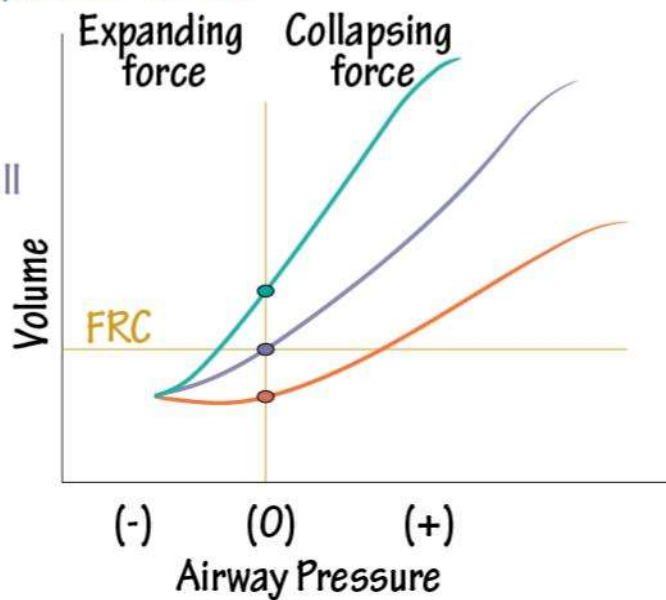
Factors Affecting Lung Compliance

Factors Increasing Lung Compliance	Factors Decreasing Lung Compliance
<ol style="list-style-type: none"> Age : Generally, younger individuals tend to have higher lung compliance due to more elastic lung tissue. Size of Lungs or Volume: Compliance is highest at FRC Lung Surfactant: Surfactant is a substance that reduces surface tension in the alveoli, promoting easier lung expansion during breathing. Normal Lung Development : Proper lung development during childhood and adolescence leads to better lung compliance in adulthood. Emphysema: In emphysema, the destruction of lung tissue can result in increased compliance but with impaired gas exchange. So the tendency of lungs to collapse is less than chest wall tendency to expand. FRC increases Mechanical Ventilation (with PEEP): Positive End-Expiratory Pressure (PEEP) during mechanical ventilation can help keep the alveoli open, improving compliance. 	<ol style="list-style-type: none"> Pulmonary Fibrosis: Scarring and stiffening of lung tissue reduce lung compliance, making it more difficult for the lungs to expand. FRC decreases in fibrosis Pulmonary Edema: Accumulation of fluid in the lungs increases tissue resistance and decreases compliance Atelectasis: Partial or complete collapse of lung tissue reduces the lung's ability to expand. Obesity: Excess body weight can impede lung expansion and decrease compliance. Chest Wall Abnormalities: Conditions affecting the chest wall, such as kyphosis or scoliosis, can restrict lung expansion. Pleural Effusion: Accumulation of fluid in the pleural space surrounding the lungs can compress and reduce lung compliance Restrictive Lung Diseases: Diseases like sarcoidosis or interstitial lung disease can limit lung expansion and decrease compliance Respiratory Muscle Weakness: Weak respiratory muscles can reduce the ability to expand the lungs fully, affecting compliance. Anaesthesia: Anaesthesia can cause a reduction in lung volume and compliance during surgery or medical procedures. Mechanical Ventilation (High PEEP): Extremely high Positive End-Expiratory Pressure (PEEP) during mechanical ventilation can reduce compliance. Pneumectomy/Lobectomy: dec compliance

Healthy vs Diseased Lungs

Compliance & FRC

- Compliance = $\Delta V / \Delta P$
Dispensability of lung, chest wall, or both.
- Healthy Lung + Chest Wall
- Lung + Chest Wall in Emphysema = Increased compliance, higher FRC.
- Lung + Chest Wall in Fibrosis = Decreased compliance, lower FRC.



SURFACE TENSION & SURFACTANT

Surface tension results from attractive forces b/w liquid molecules lining alveoli that creates a collapsing pressure directly to surface tension and inversely to alveolar radius as given below by **Laplace law** :

$P = 2T/r$. Where : P = collapsing pressure on alveolus , T = surface tension , r = radius of alveolus (cm)

1. **Large alveoli** have large radii and low pressure → easy to keep open due to decreased tendency to collapse.
2. **Small alveoli** have small radii and high pressure. So, they have tendency to collapse more
3. In the absence of surfactant: small alveoli tend to collapse (atelectasis)

SURFACTANT

- Fluid lining the alveoli and keeping them dry, synthesized by type II pneumocytes and consists of **DipalmitoylphosphatidylCholine (DPPC)**
- It Reduces surface tension by disrupting intermolecular forces b/w liquid molecules, preventing small alveoli from collapsing and inc lung compliance
- Surfactant synthesis starts around 24 weeks of gestation and it is always present at 35 weeks.
- Lecithin – Sphingomyelin ratio: (L/S ratio) > 2:1 in amniotic fluid represents mature level of surfactant
- LS ratio less than 1.5 predisposes to neonatal RDS

Neonatal Respiratory distress syndrome

- Due to lack of surfactant in premature infants, present with tachypnea, tachycardia, dyspnea and inward chest drawing with bilateral ground glass appearance of lungs.
- it can be managed by **giving surfactant via ETT** and oxygen.
- **Key word = Type II pneumocytes + DPCC + Reduce Surface tension + inc Compliance + LS Ratio + RDS**

- ✓ **Drugs that may be given via ETT** → Atropine, Epinephrine, Lidocaine , NaHCO_3 , MgSO_4 , dextrose , Salbutamol Terbutaline, dextrose , normal saline, and Acetyl cysteine.
- ✓ **Nor adrenaline is not given by ETT or ineffective through ETT.** (BCQ)

RELATION OF AIR FLOW (Q) WITH – PRESSURE (P) & RESISTANCE (R)

- Airflow is driven by and directly proportional to pressure difference between mouth/nose and the alveoli
- Inversely to airway resistance, higher the airway resistance → the lower the airflow
- $Q = \Delta P / R$ where: Q = Airflow, P = Pressure gradient and R = airway Resistance. **Mnemonics → PQR**
- **Resistance** is described by **Poiseuille law** as: $R = 8 \eta l / \pi r^4$ where η = Viscosity, l = length, r = radius of airway
- For example, if the airway radius decreases by a factor of 4, the resistance will increase by a factor of 256 (r^4)
- If airway radius is halved, resistance will increase 16 times, note the fourth power inverse relation b/w R and r
- **Major site of airways resistance is medium sized bronchioles > Medium size bronchi.**
- Smallest airways don't cause highest resistance due to parallel arrangements.
- **Parasympathetic stimulation via M2 receptors**, irritants and slow reacting substances of anaphylaxis (asthma) decrease the airway radius thereby increasing resistance to airflow.
- **Sympathetic stimulation via Beta – 2 receptors** (e.g salbutamol/isoproterenol) dilate airways and reduce R.
- High Lung volumes offer less resistance due to less traction on airways and vice versa for low lung volumes
- Asthmatics learn to breathe at higher lung volumes to offset the high airway resistance.

Respiratory System Changes in Elderly and Pregnancy

<u>Aging (Elderly)</u>		<u>Pregnancy</u>	
Remains same = TLC		Remains same = Respiratory rate + Vital capacity	
Increased	Decreased	Increased	Decreased
Lung compliance RV V/Q mismatch A – a gradient	Chest wall compliance FVC + FEV1 decreased. Ventilatory response to hypoxia or hypercapnia Poor respiratory muscle strength	Tidal volume Minute ventilation	TLC FRC RV PCO2 low due to hyperventilation (BCQ)

CONTROL OF BREATHING (BREATHING REGULATION)

- Central control → brainstem (medulla, pons) and cerebral cortex.
- Peripheral control → aortic / carotid chemoreceptors

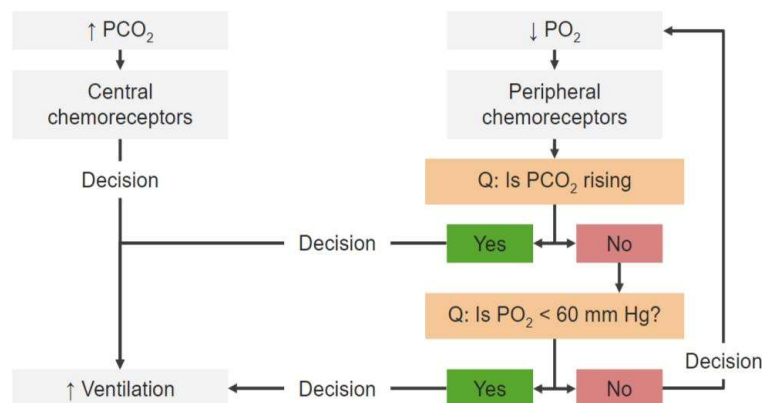
Central control

Medulla	Dorsal Respiratory group (DRG)	<ul style="list-style-type: none"> Generates the basic rhythm of breathing, responsible for Insp. Input: from Cranial Nerves IX + X Output: from Phrenic nerve to diaphragm Glossopharyngeal nerve relays information from Peripheral chemoreceptors Vagus nerve relays from both peripheral chemoreceptors and mechanoreceptors in the lung
	Ventral Respiratory group	<ul style="list-style-type: none"> Activated during exercise when expiration becomes active. Not active during normal breathing
Pons	Apneustic Centre (Lower Pons)	<ul style="list-style-type: none"> Stimulates inspiration and prolongs it by stimulating dorsal resp group, producing a deep and prolonged Inspiratory gasp i.e. apneusis. Apneustic centre is inhibited by vagus nerve and Pneumotaxic centre.

	Pneumotaxic Centre (Upper Pons) <ul style="list-style-type: none"> Shuts off the ramp signals from DRG , inhibits inspiration and prevents apneusis. So, it regulates respiratory rate ,inspiratory volume, and fine tunes respiratory rhythm. Its stimulation of DRG prevents overinflation of lungs via Hering – Breuer reflex mechanism
Cerebral cortex	<ul style="list-style-type: none"> Voluntary control of breathing to hypoventilate or hyperventilate. Hypoventilation or Breath holding is limited by resulting inc. in PCO₂ and dec PO₂ Previous period of hyperventilation may extend period of breath holding

Chemoreceptors for CO₂, H⁺ & O₂

Central Chemoreceptors (in Medulla)	<ul style="list-style-type: none"> They are present in Medullary reticular formation. Sensitive to pH (H⁺ ions) of CSF Or Interstitial fluid more than PCO₂ of arterial blood. (Low CSF pH > High Arterial PCO₂) CSF Ph matters here, not arterial blood pH. Low pH = more H⁺ ions Central receptors are Less sensitive to changes in Po₂ Keep in mind, CO₂ is lipid soluble and crosses blood brain barrier. In CSF, CO₂ + H₂O → H⁺ + HCO₃⁻¹ This resultant H⁺ directly acts on central chemoreceptors. H⁺ doesn't cross BBB as good as the CO₂ does. So, increase in Pco₂ and H⁺ stimulate breathing and vice versa for decreased Pco₂ & H⁺. CO₂ stimulates respiratory center → Hyperventilation. Or we can say acidosis stimulates Respiratory center e.g., ✓ Inj lactic acid if given will stimulate central chemoreceptor. Hyperventilation or Hypoventilation returns the Pco₂ towards normal
Peripheral Chemoreceptors (in Aortic & Carotid Bodies)	<ul style="list-style-type: none"> Aortic bodies located above and below aortic arch. Carotid bodies located at bifurcation of CCA (C4) Peripheral chemoreceptors are sensitive to: low Pao₂ > high Pco₂ > low pH (inc H⁺ ions) PH here = PH of arterial blood (not CSF) Inc. in arterial Ph+ Stimulates carotid body chemoreceptors independently of Pco₂ change. PO₂ < 60 mmHg stimulates peripheral chemoreceptors. When Po₂ is less than 60, breathing rate is specifically sensitive to Po₂. ❖ In Metabolic acidosis: breathing rate is increased because arterial H⁺ is increased and pH is decreased. So, acidosis stimulates respiratory centre as previously mentioned. ❖ Past paper BCQ : ❖ What stimulates CNS → Prefer CO₂ > Acidosis. Both receptors respond well to → Pco₂



Other Types of Receptors for Breathing Control

Lung stretch receptors	Irritant receptors	Juxtacapillary (J) receptors	Joint & Muscle receptors
located in smooth muscles of airways. Lung distension → stimulates these stretch receptors, they produce decrease in breathing frequency → called Hering – Breuer reflex	Located b/w airways epithelial cells. Stimulated by noxious substances e.g., dust and pollens (BCQ)	Located in alveolar cells close to capillaries. They cause rapid shallow breathing upon stimulation by capillaries engorgement (e.g., LHF)	Activated during limbs movement. Involved in early stimulation of breathing during exercise . So, breathing during exercise is maintained via Proprioception (BCQ)

PULMONARY CIRCULATION & DIFFUSION OF GASES

- Pulmonary circulation is a low resistance + high compliance system.
- Hypoxia causes Vasoconstriction here (exception)
- Diffusion rates for O₂ & CO₂ depend upon partial pressure differences across membrane + area available for diffusion.
- Gas diffusion is according to **Fick's law** → $V_x = DL - \Delta P$
- V_x** is vol of gas , **DL** is **lung diffusion capacity** , /**ΔP** is partial pressure difference.
- DL is measured with Carbon mono-oxide.**
- DL** is equivalent to permeability of alveolar pulmonary capillary barrier, inversely to thickness of barrier and directly proportional to surface area + diffusion co-efficient of gas.
- DL Increases** : in **exercise** (as more capillaries are open so more surface area)
- DL decreases** : in **Emphysema** (decreased surface area), **Fibrosis & Pulmonary Edema** (increased diffusion distance)

Diffusion Limited Exchange:

- Gas** Rapidly delivers into blood vessels, encounters resistance during diffusion into tissues, therefore diffusion into tissue is a limiting factor. They are not ideal for medical imaging – contrast.
- In Emphysema → surface area for diffusion is decreased, so O₂ diffusion decreases.
- In fibrosis → thickening of alveolar membrane increases diffusion distance thereby reducing O₂ diffusion
- Gas doesn't equilibrate by the time blood reaches the end of lung capillaries** because partial pressure difference of gas b/w alveolar air and pulmonary capillary is maintained.
- Diffusion limitation Produces early hypoxia than hypercapnia.

Perfusion Limited Exchange:

- Gas** - limited delivery into vessels → so delivery to tissues is the limiting factor but it diffuses rapidly into tissues making them better suited for medical imaging techniques.
- The diffusion of perfusion limited gas can be increased if blood flow increases** because the **gas equilibrates** early along length of lung capillaries and partial pressure of gas in arterial blood = partial pressure in alveolar air.

Diffusion Limited exchange	Perfusion limited exchange
1. O ₂ (emphysema, fibrosis, strenuous exercise)	1. O ₂ – normal conditions
2. CO (BCQ)	2. CO₂ (BCQ)
3. CH ₄ – Methane	3. N ₂ O

OXYGEN TRANSPORT

O₂ is carried in blood in 2 forms: dissolved form Or **Hb-bounded form (most imp)**

HAEMOGLOBIN:

- Female: 12 – 16 g/dL
- Male: 14 – 18 g/dL
- **Adult Hb (α₂β₂):** composed of 4 polypeptide chains (2 alpha + 2 beta) each of which binds 1 molecule of oxygen.
- **Fetal Hb (HbF):** 2 alpha +2 gamma chains (**α₂γ₂**)
- **Myoglobin** has single polypeptide chain and higher O₂ affinity than Hb.
- Hb increases the O₂ – carrying capacity of blood by **70** times.
- The protein component acts as buffer for H⁺ ions.
- Iron is in the ferrous form (Fe²⁺) which binds O₂, whereas in Methaemoglobin Fe³⁺ present → no O₂ binding but high affinity for Cyanide causing tissue hypoxia from low SaO₂ and low O₂ content.
- Normally 1 g Hb binds 1.34 mL O₂ (normal Hb on avg is 15 g/dL).
- O₂ content = (1.34 × Hb × SaO₂) + (0.003 × PaO₂). It includes both bound and dissolved O₂ (Unbound form)
- O₂ binding capacity ≈ 20 mL O₂/dL of blood. O₂ delivery to tissues = CO × O₂ content of blood (as given above)

Remember that:

- No change in O₂ saturation occurs in anemia and Polycythemia. Only O₂ content varies e.g., dec in anemia.
- CO poisoning : Decreased O₂ sat.
- In Methemoglobinemia → low O₂ sat + low O₂ content as well
- In CN poisoning: Hb conc. , O₂ sat, O₂ content and dissolved Oxygen = All Normal

HB – O₂ DISSOCIATION CURVE (ODC)

ODC describes relationship b/w percentage of saturated Hb and partial pressure of O₂ in blood.

Hb is an allosteric protein that exhibits +ve co-operativity when binding to O₂ such that:

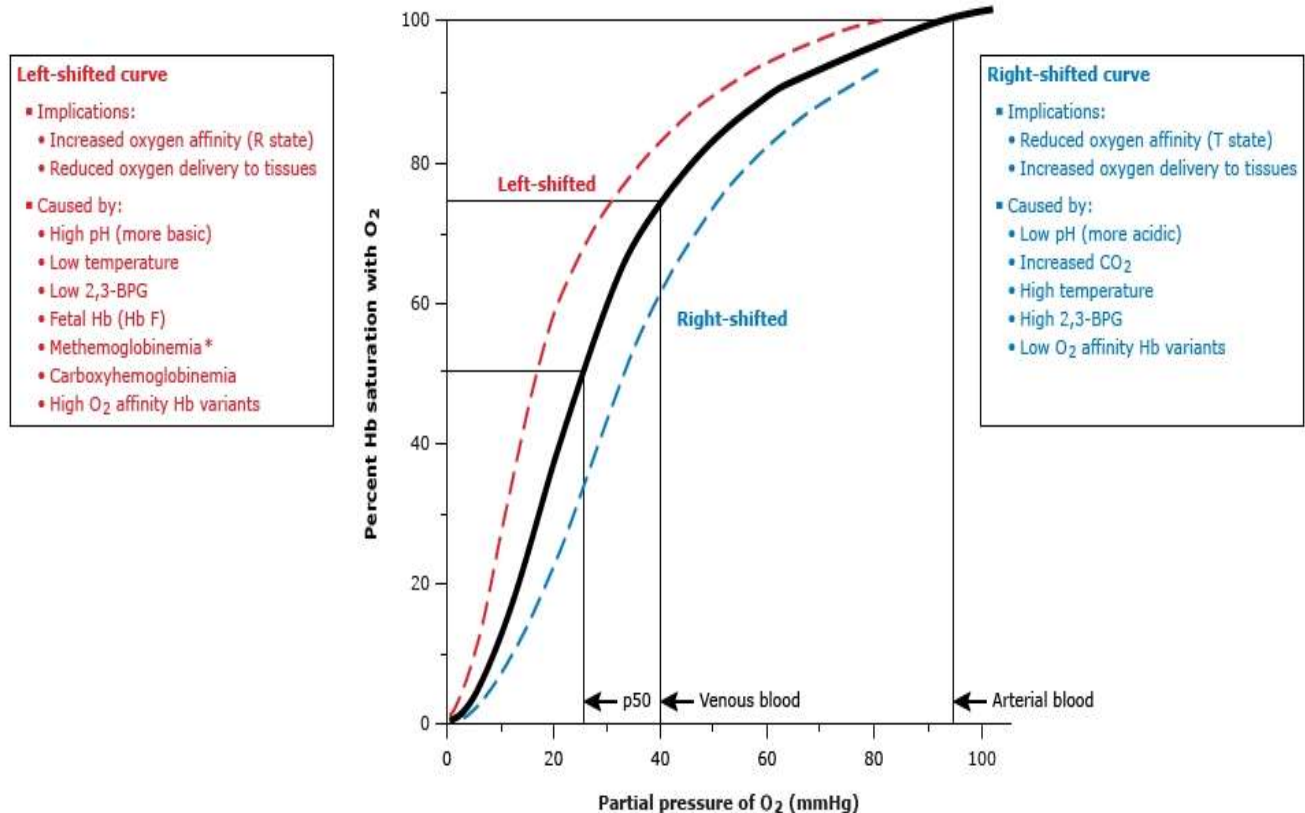
1. Oxygenated Hb has high affinity for O₂ (300 times).
2. Deoxygenated Hb has low affinity for O₂ → promotes release/Unloading of O₂.
3. Due to +ve co-operativity, tetrameric Hb molecule can bind 4 O₂ molecules and has higher affinity for each subsequent O₂ molecule bound. So the curve becomes **SIGMOIDAL** shape.
4. This 4th O₂ molecule has highest affinity. This change in affinity facilitates loading of O₂ in lungs and unloading O₂ at tissues. Myoglobin curve is Hyperbolic form due to lack of +ve co-operativity and being monomeric.
5. Pulse Oximetry measures % Hb saturation in arterial blood by dual wavelength spectrophotometry
PaO₂ can be measured from ODC using the measured % saturation.
6. ODC is not affected by Hb concentration.

At Po ₂ of 100 mmHg (Arterial blood)	At Po ₂ of 40mmHg (Mixed venous blood)	At Pao ₂ of 25mmHg
<ul style="list-style-type: none"> • Hb – 100% saturated • O₂ bound to all 4 Heme groups on Hb 	<ul style="list-style-type: none"> • Hb – 75% saturated • O₂ bound to ¾ heme groups 	<ul style="list-style-type: none"> • Hb – 50 % saturated • Pao₂ at 50% sat is the P50. • O₂ bound to 2/4 heme molecules. • Right shift - ODC: P50 = 35 mmHg • Left shift of ODC: P50 = 15 mmHg

Changes In ODC

Right shift of ODC	Left shift of ODC
<p>Rt shift = low O₂ affinity of Hb leading to inc Unloading of O₂ in tissues → Bohr's effect</p> <p>Factors causing right shift are:</p> <p>Mnemonics Right = More</p> <ol style="list-style-type: none"> 1. Inc Temperature (e.g exercise) 2. Inc H⁺ ions i.e acidosis (Low pH) 3. Inc Co₂ – Bohr's effect 4. Inc 2,3-Biphosphoglycerate (2,3-BPG) 5. High Altitude 	<p>Left shift = high O₂ affinity leading to decreased unloading of O₂ in tissues and displaces Co₂ from blood → Haldane's effect</p> <p>Mnemonics Left = Less</p> <ol style="list-style-type: none"> 1. Low temperature 2. Low PCO₂/H⁺ (alkalosis – high pH) 3. Low 2,3-BPG 4. HbF, Methemoglobin 5. CO poisoning → extreme left shift of ODC as CO has 200 – 250 Times more affinity for Hb than O₂

2,3 BPG: present in RBCs and enhances ability of Rbcs to release O₂ into tissues by interacting with beta chains of Hb causing low affinity for O₂ and increase release/unloading of O₂.



CO₂ TRANSPORT

CO₂ is transported from tissues to lungs in 3 forms:

1. **HCO₃⁻¹** : majority of blood Co₂ (70%) is carried as Hco₃ in plasma. HCO₃/Cl transporter on RBC membrane allows Hco₃ to diffuse out to plasma and Cl to diffuse into RBCs → Chloride shift

$$\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^{-1}$$

$$\text{H}^+ + \text{Hb} \rightarrow \text{HHb}$$
2. **Carbaminohemoglobin or Hbco₂** (21- 25%): Co₂ bound to Hb at N- terminus of globin (not Heme).
3. **Dissolved Co₂** (5-9%)
Haldane Effect in Lungs: oxygenation of Hb in lungs promotes dissociation of H⁺ from Hb. This causes more CO₂ formation : $\text{H}^+ + \text{HCO}_3^{-1} \rightarrow \text{CO} + \text{H}_2\text{O}$.
 Therefore, CO₂ is released from RBCs → Haldane's effect

Alveolar Gas equation

- **PACO₂ = $\frac{\text{PIO}_2 - \text{Paco}_2}{R}$**
- PACO₂ = alveolar PCO₂, piO₂ = Po₂ in inspired air, PaCO₂ = arterial pCO₂
- R is respiratory Quotient = Co₂ produced / O₂ consumed
- PAO₂ = 150 mmHg – PaO₂/0.8
- A-a gradient = $\frac{\text{age}}{4} + 4$
- **A – a gradient increases** in aging, V/Q mismatch, R to L shunt and diffusion defects

OXYGEN DEPRIVATION

	Causes of Hypoxia: decrease CO, hypoxemia, ischemia, anemia, and poisoning (CO/CN)			
Hypoxia	Hypoxic Hypoxia	Anemic Hypoxia	Stagnant Hypoxia	Histotoxic Hypoxia
Decreased O2 Delivery to Tissues	Decrease O2 tension. Examples High Altitude V/Q mismatch	Decrease O2 carrying. Anemia CO poisoning Arterial PaO2 is normal	Low perfusion Heart failure Shock	Not able to use O2. Cyanide poisoning
	A – a gradient is used to measure cause of hypoxemia			
Hypoxemia	Normal A – a gradient (0 - 10 mmHg)		Increased A – a gradient (>10 mmHg)	
Decreased Arterial O2 (Pao2)	O2 doesn't equilibrates b/w alveolar gas and arterial blood ❖ High altitude ❖ Hypoventilation e.g obesity , Opiods use and hypoventilation syndromes		O2 equilibrates b/w alveolar gas and arterial blood ❖ R → left shift ❖ V/Q mismatch ❖ Diffusion limitation (e.g fibrosis)	
Ischemia	Causes of Ischemia are :			
Loss Of Blood Flow	1. Impeded arterial flow. 2. Decreased venous drainage			

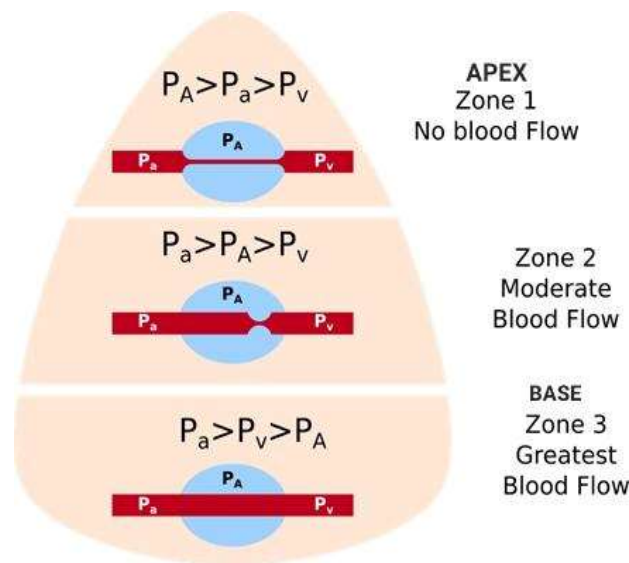
ZONES OF LUNGS

Classically, the lung Has been divided into 3 different zones:

Zone 1: No blood flow during all portions of the cardiac Cycle because the local alveolar capillary Pressure never rises higher than the alveolar air pressure during any Part of the cardiac cycle. $P_A \geq P_a > P_v$

Zone 2: Intermittent blood flow only during the peaks of Pulmonary arterial pressure because the systolic pressure is Greater than the Alveolar air pressure, but the diastolic pressure is less than the Alveolar air pressure.

Zone 3: Continuous blood flow because the alveolar capillary Pressure remains greater than alveolar air pressure during this. $P_a > P_v > P_A$



- Zone 1 is not seen in normal lungs, present in hemorrhage/ Positive Pressure ventilation.
- Normal lungs have Zone 2 + Zone 3
- In Zone 2 blood flows due to difference of arterial and alveolar oxygen.
- **At apex:** Both ventilation and perfusion are low but Perfusion is poor as compared to ventilation, PO_2 is highest, PCO_2 is lowest \rightarrow efficient gas exchange occurs (V/Q at apex = 3 – wasted ventilation)
Due to efficient gas exchange Mycobacterium Tb grow in apices of lungs
- **At Base:** Both Ventilation and perfusion are higher, but perfusion is greater than ventilation, PO_2 is lowest, PCO_2 is highest \rightarrow less efficient gas exchange
 V/Q at base = 0.6 (wasted perfusion)
- V/Q at middle zone is approx. 1. Also $V/Q = 1$ is exercise
- V/Q is below normal in airway obstruction ($V/Q = 0$ in Shunt)
- **V/Q is infinity in:** Blood flow obstruction (Pulmonary embolism) \rightarrow physiological dead space
- 100% $O_2 \rightarrow$ improves blood flow in Pulmonary embolism but not effective in airway obstruction

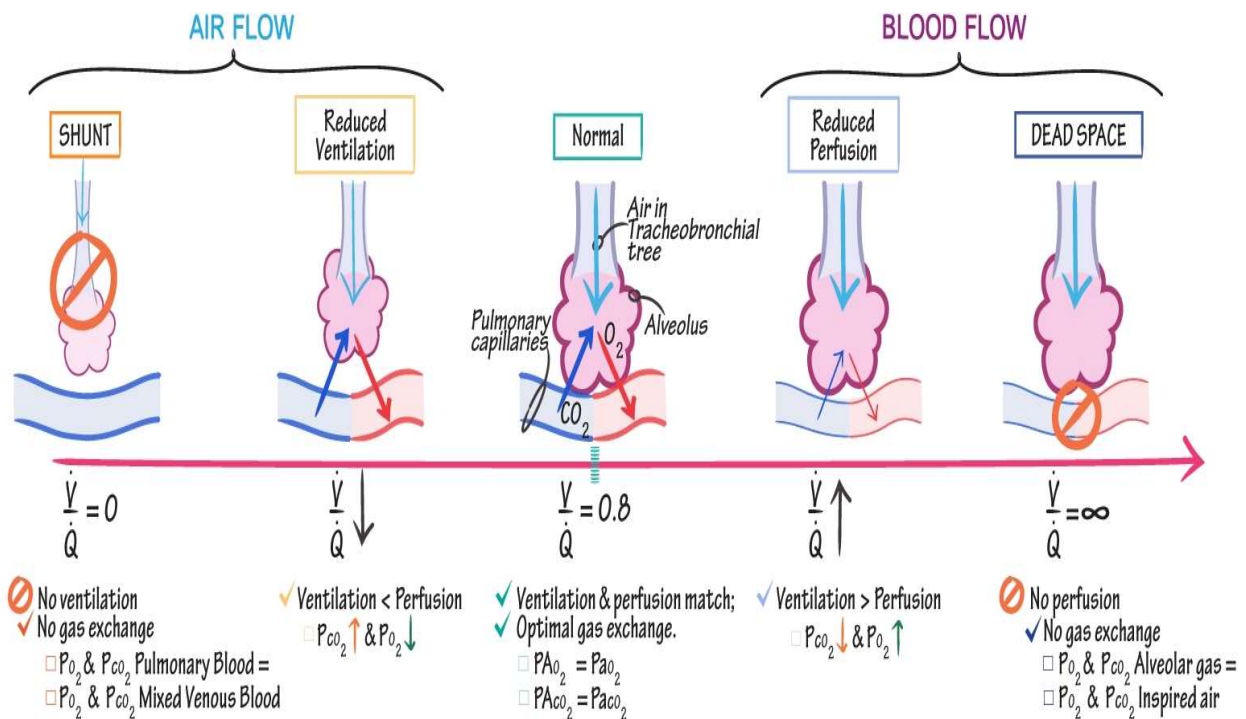
Zone	Ventilation (V)	Perfusion/Blood flow (Q)	V/Q	PO_2	PCO_2
Zone 1 (Apex)	Lower	Lowest	Highest (0.3)	Highest 130 mmHg	Lower 28 mmHg
Zone 2 (Middle)	Moderate	Moderate	1	--	--
Zone 3 (Base)	Higher	Highest	Lowest (0.6)	Lowest 89 mmHg	Higher 42 mmHg

Imp Concepts

Shunt: $V/Q = 0 \rightarrow PO_2$ and PCO_2 of Pulmonary blood = Po_2 & Pco_2 of Mixed Venous blood. NO Gas exchange.

Dead space: $V/Q = 1/\infty$ (infinity) $\rightarrow Po_2$ & Pco_2 of alveolar gas = Po_2 & Pco_2 of inspired air. NO Gas exchange.

Right-to-left shunts (PaO ₂ low)	Left-to-right shunts (high PaO ₂)
<ul style="list-style-type: none"> Normally occur to a small extent because 2% of the cardiac output bypasses the lungs. They are seen in tetralogy of Fallot. Always result in a decrease in arterial Po_2, because of the admixture of venous blood with Arterial blood. The magnitude of a right-to-left shunt can be estimated by having the patient breathe 100% O₂ and measuring the degree of dilution of oxygenated arterial blood by deoxygenated shunted (venous) blood. 	<ul style="list-style-type: none"> They Are more common than are right-to-left shunts because pressures are higher on the left Side of the heart, Are usually caused by congenital abnormalities (e.g., patent ductus arteriosus) or traumatic injury L to R shunts Do not result in a decrease in arterial Po_2, Instead Po_2 will be elevated Of the heart because there has been admixture of arterial blood with venous blood



ADAPTATIVE RESPONSES TO HIGH ALTITUDE & EXERCISE

Response	High Altitude	Exercise
Increased	<ol style="list-style-type: none"> 1. Ventilation – hyperventilation 2. PH inc – Resp alkalosis 3. Hb conc. Inc – inc EPO 4. 2,3- BPG raised – right shift of ODC - O₂ released. 5. Pulmonary vascular resistance raised – due to hypoxic vasoconstriction → leads to pulmonary HTN and RVH 	<ul style="list-style-type: none"> ○ O₂ consumption ○ CO₂ production ○ Ventilatory rate ○ Pulmonary blood flow ○ Inc Venous Pco₂ ○ Right shift of ODC
Decreased	<ol style="list-style-type: none"> 1. Alveolar PO₂ low, - due to dec barometric pressure 2. Arterial PO₂ decreased (hypoxemia) 	<ul style="list-style-type: none"> ○ dec venous O₂
Remains same	----	Arterial Pco ₂ & PO ₂ – no change Arterial pH = No change in moderate exercise, low in strenuous exercise

Key Facts

- **Hypoxia causes Pulmonary vasoconstriction whereas Hypoxia in all other systems causes vasodilation.**
- Hypoxia stimulates synthesis of hypoxia inducible factor which increases mRNA for Erythropoietin → inc Hb + inc Hematocrit.
- Alveolar ventilation during exercise is maintained via collateral stimulation from higher centres.
- If alveolar ventilation is halved → Pco₂ is doubled (due to hypoventilation)
- Difference between systemic and pulmonary circulation = Low resistance in the pulmonary Circulation
- Venous and arterial Po₂ and PCO₂ are same on the dorsum of the warm hand.
- Bronchial spasm physiologically present at early morning. Symptoms of asthma are usually Worse at night and in the early morning or in response to exercise or cold air.
- The umbilical vein of the fetus like the pulmonary vein of the adults carries the circulation most Highly oxygenated blood.

MISCELLANEOUS TOPICS (Sometimes Asked in Exams)

Fraction of inspired oxygen (FiO₂)

maximum dose, which does not cause fetolental adrenoplasia is 1 and this is also the safest dose in the pregnant lady

It is unaffected by FiO₂ intrauterine. So 0.65 is wrong (in most MCQs book). Dose can be given upto 1 .

For any given level of exercise, oxygen consumption is higher in pregnant than in non-pregnant Women

O₂ debt:

Oxygen debt is the amount of extra oxygen that must be taken after exercise to restore The muscles to the resting condition. When a person stop exercising, the rate of oxygen uptake does not immediately return to Pre-exercise level, it returns slowly. This extra oxygen is used to repay the oxygen debt incurred during exercise

- The early portion of oxygen debt is called **alactacid oxygen debt and amount to about 3.5Liters.**
- The latter portion is called the lactic acid oxygen debt and amount to about 8 liter

Pulmonary Artery: It Supplies alveoli, Highest blood velocity, the highest content of CO₂

- Contain Highest mixed venous blood. O₂ dependent K⁺ channel are present in the pulmonary artery
- The Pulmonary artery pressure increase in hypoxia because hypoxia cause vasoconstriction
- Pulmonary vasoconstriction occurs due to reduced systemic (arterial) PO₂
- Saddle emboli cause sudden death by blocking pulmonary arteries

O₂ Level Differences

- ❖ Highest Po₂ in pulmonary capillaries and lowest in the umbilical artery
- ❖ Highest O₂ saturation = Umbilical Vein (note the difference in above and this point – tested in exam)
- ❖ Highest venous O₂ saturation in the renal vein
- ❖ Highest O₂ tension present in pulmonary capillaries
- ❖ Less in the fetus than mother = PCO₂
- ❖ Oxygen is taken up to lung through simple diffusion.
- ❖ Lowest O₂ level in = SVC
- ❖ PO₂ at sea level in normal adult is 97%
- ❖ Lowest capillary permeability in Brain and Most permeable capillaries are in kidney.
- ❖ Glomerular capillary has the highest pressure because of- short Afferent arteriole.
- ❖ Reduction in blood supply to brain causes seizure.
- ❖ HCO₃ that rises with 10mm Hg of PCO₂ is 3
- ❖ When Hb is low → no changes in O₂ sat and PaO₂ but dec O₂ content of arterial blood occurs
- ❖ The most common cause of cell injury worldwide is hypoxia.
- ❖ Oxygen level in the blood will decrease in hypoxic hypoxia.
- ❖ Alveolar ventilation is 4.2 L/min.

Methemoglobinemia

- ❖ presents with cyanosis that doesn't increase with O₂ and chocolate color blood
- ❖ It is helpful in treating CN poisoning
- ❖ It can be Treated with methylene blue and vitamin C

CO Poisoning	Cyanide Poisoning
<ul style="list-style-type: none"> ❖ Colourless and odourless gas ❖ Source: Motor exhaust, gas heaters and fire arm victims ❖ Multiple victims may be involved (faulty furnaces) ❖ Hb has 250 times more affinity to bind with CO as compared to O₂ → Carboxy-Hb → dec O₂ sat of Hb ❖ shifts the oxy-Hb curve to left (extreme Left shift) due to inc affinity for O₂ → dec O₂ Unloading in tissues ❖ It also inhibits Cytochrome oxidase ❖ Arterial PaO₂ is normal, elevated Carboxyhemoglobin on co- oximetry ❖ On MRI: Bilateral globus pallidus lesion ❖ When there is 70% carbon monoxide Hb in blood, death occurs. Cherry red skin with bullous lesion is present ❖ Presents with: Headache, vomiting, confusion, visual disturbance, and coma. ❖ Treated with 100% O₂ or Hyperbaric Oxygen (HBO) if severe 	<ul style="list-style-type: none"> ❖ Exposure from Synthetic product combustion, cyanide ingestion (suicidal attempts), firearm victims, amygdalin ingestion (in apricot seeds) ❖ Presents with: Headache, dyspnea, drowsiness, seizure, coma, cherry red skin with bitter almond odour. ❖ Arterial PaO₂ is normal, raised lactate → Met acidosis ❖ ODC – Normal but inability to use O₂ due to ineffective oxidative phosphorylation. ❖ Management: Decontamination Nitrites: Oxidized Hb → Methemoglobin, binds CN to form cyanomethemoglobin which dec Toxicity. Inc Renal excretions by: Hydroxocobalamin (binds CN to form cyanocobalamin → renal excretion Sodium thiosulfate: inc CN conversion to thiocyanate → renal excretion

Capnometer: A Monitoring device that measures and numerically displays the concentration of carbon Dioxide in exhaled air.

Radford nomogram: It is used to predicate necessary tidal volume for artificial respiration on the basis of Respiratory rate, body weight and sex.

Effect of Transaction at various level

1. **Injury Above pons** : regular breathing
2. **Injury Below medulla** → respiration stop (phrenic nerve cut)
3. **Injury Below Pneumotaxic center**: sustained inspiration apneusis with the vagal Cut. However, if the vagus is intact, respiration is continuous.
4. **Injury Below Apneustic center**: gasping type irregular respiration continues, with Or without our vagus

Concept of various pressures in Resp system

1. **Intrapleural pressure** (also called intrathoracic pressure)

refers to the pressure within the pleural Cavity. Normally, the pressure within the pleural cavity is slightly less than The Atmospheric pressure, in what is known as negative pressure. It represents the pressure in the thin film of fluid between the lung and chest wall

- **Causes of negativity of intrapleural pressure**: The Lymphatic system drains the pleural fluid, generating a negative intra-pleural pressure (-2 mm Hg)
- **Measurement of intra-pleural pressure**: can be measured directly by introducing a needle to the Pleural cavity or by the indirect method by introducing the oesophageal balloon into Esophagus
- **Significance of intra-pleural pressure**: Prevents the collapsing tendency of lungs. Increases the venous return

2. **Atmospheric pressure**:

The pressure of the air around us. At sea level the atmospheric pressure is 760 mm Hg, at Higher altitude, the pressure is lower

3. **Intra-pulmonary pressure**:

The pressure within the bronchial tree and alveoli. The pressure fluctuates below and above atmospheric pressure during each cycle of breathing.

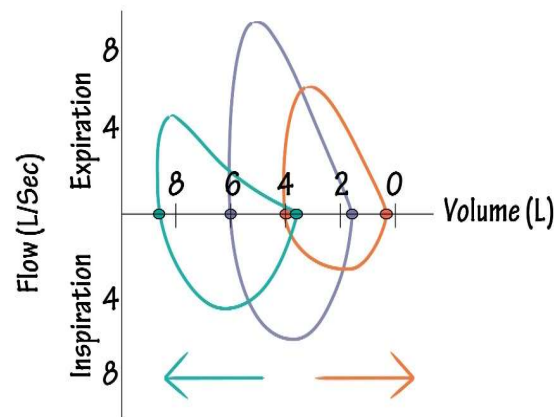
4. **Sub atmospheric pressure (-)**

It act as a force to prevent collapse the lung

- During normal restful breathing, intrapleural pressure is always sub atmospheric (or Negative) and thus act as a force to expand the lung
- At the end of expiration, intrapleural pressure is sub atmospheric.
- During inspiration intrapulmonary pressure drops below atmospheric pressure (-1mm Hg). Airflows into the lungs, down the pressure gradient, until intrapleural pressure = Atmospheric pressure.
- During expiration, intra-pulmonary pressure rises above atmospheric pressure (+1 mm Hg). Gases flow out of the lungs, down the pressure gradient, until intra-pulmonary Pressure is 0.
- Lung collapse is prevented by: adhesion of the pleural membrane .
- During Spontaneous ventilation, the body maintain a residual volume in Its lungs to prevent them from collapse.

DISEASES OF RESPIRATORY SYSTEM

Flow – Volume Parameter	Obstructive Lung diseases	Restrictive Lung diseases
TLC , FRC , RV	increased	Decreased
FEV1	More decreased than FVC	Decreased
FVC	Decreased	Decreased
FEV1/FVC	Decreased (less than 0.8)	Normal or increased ratio (≥ 0.8)
Direction of Flow- Vol Loop	Left shift	Right shift
Examples of Obs vs Restrictive lung diseases		
Obstructive lung diseases: Asthma, COPD (Emphysema, Chronic bronchitis) and bronchiectasis		
Restrictive lung diseases:		
1. Altered respiratory mechanism → Extra pulmonary diseases with normal DLCO and normal A – a gradient. i. Chest wall anomalies (Scoliosis) ii. Polio, myasthenia, GBS and ALS 2. Diffuse parenchymal lung diseases/Interstitial lung diseases: Pulmonary diseases, raised A-a gradient + DLCO. Occupation lung disease: Pneumoconiosis (Coal worker pneumoconiosis, Silicosis and asbestosis) Sarcoidosis, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, ARDS , Granulomatosis with polyangiitis, Drugs induced fibrosis (Busulfan, bleomycin , amiodarone and methotrexate).		

Dynamic Flow-Volume Loops

Obstructive: Loop shifts Left,
Volumes are > than normal;
FEV1 decreases more than FVC
(lower FEV1/FVC).

Restrictive: Loop shifts Right;
Volumes are < than normal.
FEV1 and FVC decrease in proportion
(normal or even elevated FEV1/FVC)

OBSTRUCTIVE LUNG DISEASES

Obstruction of airflow (↑ FRC, ↑ RV, ↑ TLC) leads to air trapping in lungs with premature airway closure at high lung volumes (↓ FEV1, ↓ FVC, ↓ FEV1/FVC ratio). Leads to V/Q mismatch (V/Q below normal)

ASTHMA

Type 1 hypersensitivity reaction (IgE) In \pm genetically predisposed individuals with combination of environmental factors like allergens (dust/pollens), stress, exercise or cold leading to chronic inflammation + hypersensitive airways.

Types

1. **Extrinsic asthma (Atopic 70%)**: immune mediated, family history +ve, disease begins in childhood. Common triggers: **dust, pollens, food**. **Subtypes** of extrinsic asthma include atopic, occupational asthma and allergic bronchopulmonary aspergillosis (ABPA).
2. **Intrinsic asthma (30%)**: initiated by diverse non – immune mechanism like viral infection (most common), chemical irritants, drugs (aspirin), pollutants, cold, stress and exercise. No family history present and disease begins in later life mostly after URTI by Viruses etc.

Pathogenesis & Findings:

- Hyperresponsive bronchi \rightarrow reversible bronchoconstriction, Smooth muscle hypertrophy + hyperplasia
- **Curschmann spiral**: shed epithelium forms whorls of mucous plugs
- Charcot – Laden crystals: eosinophilic hexagonal crystals formed by eosinophils breakdown in sputum.
- **Triad of: Cough + Wheeze + dyspnea**. DLCO is normal or raised. **Asthma effect Medium sized bronchioles.**
- Tachypnea, hypoxemia and pulsus paradoxus in acute cases (status asthmaticus)
- **NASID/Aspirin related asthma is due to overproduction of leukotrienes via COX inhibition.**
- Samter's triad = Aspirin allergy + asthma + nasal polyps.
- **In chronic asthma: increase lymphocytic response to mitogens play role in pathogenesis.**
- IL – 13 gene polymorphism has been found to be linked with asthma
- Diagnosis via: Spirometry – FEV1 \pm Methacholine challenge test.

Management of Asthma:

1. **B2 – agonists**: short acting (SABA) - salbutamol, albuterol, long acting (LABA) – salmeterol, formoterol
2. **Steroids**: inhaled (1st line in chronic asthma) – fluticasone, budesonide
3. **Muscarinic antagonist**: ipratropium, tiotropium. Also used in COPD
4. **Anti – leukotrienes**: CysLT1 leukotriene receptor blockers \rightarrow montelukast, zafirlukast
5 – Lipoxygenase inhibitor: Zileuton \rightarrow blocks arachidonic acid to leukotrienes conversion.
5. **Methylxanthines** (theophylline): inhibits phosphodiesterase, may cause arrhythmias.
6. **Mast cells stabilizers**: Cromolyn, nedocromyl, prevent mast cell degranulation.
7. **Anti IgE monoclonal antibody**: Omalizumab.
8. **Anti IL – 5 monoclonal therapy**: reslizumab, benralizumab, mepolizumab.

Step - wise Management				
Step 1	Step 2	Step 3	Step 4	Step 5
Inhaled SABA as required	Inhaled SABA 400mcg/day	Add LABA If good response – Continue LABA If inadequate control – add inhaled steroids (LABA + Steroids 800mcg/d) If no response to LABA: Stop LABA and inc inhaled steroids dose If still not beneficial: Add montelukast/ theophylline.	Inhaled steroids dose 2000mcg/d Add a 4 th drug like Leukotriene antagonist.	Oral steroids. Consider other options like Omalizumab. Give inhaled steroids dose: 2000mcg/d
Management of Status Asthmaticus (O – SHIT)				
1. Oxygen. 2. Inhaled Beta -agonist. 3. IV Steroids (hydrocortisone) 4. Ipratropium 5. IV Theophylline Ipratropium may be used if unresponsive to beta 2 agonists. Muscarinic antagonists don't cause bronchodilation, but they prevent bronchoconstriction				

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

- COPD includes emphysema and chronic bronchitis.
- The symptoms of these 2 overlap each other and may coexist in an individual.

Risk Factors:

1. **Smoking:** in 70-80%, cases, most imp risk factor is smoking. Smoking cessation is most effective management strategy – halts disease progressive + reverses changes in respiratory tract.
2. **Genetic factors:** alpha – 1 antitrypsin deficiency is linked to panacinar emphysema
3. **Environmental and occupational factors:** pollutants, chemicals e.g fumes
4. **Asthma:** chronic asthma may predispose to COPD
5. **Recurrent respiratory infections:** increases the chances of chronic bronchitis.

Classification of Severity of Airflow Limitation in COPD

- In patients with FEV1/FVC < 0.70 (Post – bronchodilation FEV1)
- **GOLD = Global initiative for chronic obstructive lung diseases**
- GOLD 1 (mild): FEV1 = 80% predicted
- GOLD 2 (moderate): 50% = FEV1 < 80% predicted
- **GOLD 3 (severe):** 30% = FEV1 < 50% predicted
- GOLD 4 (very severe): FEV1 < 30% predicted

EMPHYSEMA

(Pink Puffers)

(Permanent dilatation and destruction of distal small airways leading to dec elastic recoil + inc compliance)

Types: According to pulmonary lobule involvement divided into following types.

- **Centriacinar/Centrilobular:** strong link with smoking, affects upper lobe.

affects respiratory bronchioles sparing distal alveoli

smoking → inc elastase activity, imbalance of proteases and anti – proteases, leads to loss of elastic fibres and increased lung compliance. Smoking also attracts neutrophils, macrophages and CD8+ cells which cause chronic inflammation. which further release elastase.

Nicotine → inc neutrophils elastase activity (BCQ)

- **Panacinar/Panlobular:** Due to alpha – 1 antitrypsin deficiency, affects lower lobes.

Affects entire acinus (respiratory bronchioles + alveoli) till terminal bronchioles.

- **Distal acinar/Paraseptal:** affects upper lobes, linked to smoking, involves areas adjacent to pleura and lining of lungs. The rupture of small airways may lead to spontaneous pneumothorax.

Typical features of emphysema are:

- Smoker with Barrel shaped chest (↑ AP Diameter), Pursed lip breathing (To inc airway pressure and prevent lung collapse)
- Hoover's sign → pronounced inward chest movement on inspiration
- muscle wasting and respiratory fatigue. Clubbing is not a feature of COPD.
- ↓ DLCO due to destruction of alveolar walls and low blood volume in capillaries
 - **DLCO increases in Polycythemia** > asthma (BCQ)

Complications: Hypoxemia, resp acidosis, Cor pulmonale, RHF and death.

Management: O2, bronchodilators, ipratropium, steroids and antibiotics.

CHRONIC BRONCHITIS (Blue Bloaters)

Productive cough ≥ 3 months in a year for > 2 consecutive years.

Hypersecretion of mucous due to hypertrophy + hyperplasia of mucous secreting sub mucosal glands in bronchi.

Reid index = Thickness of mucosal gland layer/ thickness of wall b/w epithelium & cartilage.

Normal REID index must be less than 0.4 (40%). It increases to > 0.5 (50%) in bronchitis.

Presents with: Wheeze, crackles, cyanosis, SOB, CO2 retention, Polycythemia

Normal DLCO despite Polycythemia.

BRONCHIECTASIS

- Chronic necrotizing infection of bronchi/obstruction leads to permanently dilated airways. Affects lower lobes mostly.
- **Causes:** associated with bronchial obstruction, immotile cilia (smoking/kartagener

- syndrome), cystic fibrosis (MCC in USA), Tumors, foreign body or allergic bronchopulmonary aspergillosis.
- **Childhood incidence of Measles or whooping cough** is also associated with this disease.
- Presents with cough + sputum + hemoptysis + clubbing + recurrent infections (pseudomonas)
- **HRCT chest – gold standard**, shows **tram track sign/honey comb** appearance.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Key Points

- ✓ Pathology
 - Chronic, progressive, irreversible
 - Air Flow Obstruction -> High Lung Volumes (FRC, RV, TLC).
 - Reduced FEV1/FVC
 - Chronic Bronchitis
 - Small Airway Disease
 - Emphysema
- ✓ Asthma-COPD overlap syndrome:
 - Airway hyperreactivity + COPD
- ✓ V/Q mismatch, hypoxemia, pulmonary hypertension, Right heart failure
- ✓ Demographics:
 - ~16 million diagnosed in U.S.; a leading cause of death globally.
 - Men & Women, < 65, Smokers (past or present)
- ✓ Risk factors:
 - Smoking, air pollution, genetics.
 - Alpha-1 antitrypsin deficiency; allows excess Elastase, which degrades alveoli.
- ✓ Treatment:
 - Bronchodilators, Steroids, Resp. therapy, Oxygen.

COPD = Air Trapping

Reduced elastic recoil in parenchyma (emphysema)
Increased airway resistance (chronic bronchitis, SAD)
Most patients have a combination!

Signs & Symptoms

- ✓ Decreased breath sounds
- ✓ Cough, Sputum, Wheezing, Dyspnea
- ✓ Rhonchi from airway secretions
- ✓ Pursed-lip breathing
- ✓ Tripod position
- ✓ Cyanosis

High Lung Volumes: Hyperinflation

- Diaphragm flattens, accessory resp. muscles must do more work.
- Barrel-shaped chest
- Hoover's chest sign
Pronounced inward movement of costal margin during inspiration.

Weight loss & muscle wasting

Peripheral edema

- Right heart failure
- Reduction in renal flow

Systemic inflammation

Exacerbations —

- ✓ Acute bouts of worse symptoms that require treatment changes.
- ✓ Infections, air pollutants.

Pathology

Smoking: Increased mucus production, Impaired ciliary clearance, Oxidative stress, and Inflammatory cell recruitment.

Chronic Bronchitis

Chronic cough + sputum for 3+ mos. in 2 years.

- Mucus: Abundant, thick.
- Respiratory epithelium: More goblet cells, impaired cilia, poss. squamous metaplasia.
- Submucosa: Inflammatory cell infiltration
- Smooth Muscle: Hypertrophy
- Mucosa: Hypertrophy & Hyperplasia of mucous glands

Small airway disease

Significant airflow resistance.

- Mucus plugging, inflammation, airway remodelling, fibrosis & thickening.
- Variation in V/Q

Emphysema

Inflammatory cells secrete elastase, which breaks down alveolar walls; oxidative stress damages collagen and elastin.

- Less elastic recoil -> Lower driving force to expel air.
- Loss of support -> airways collapse & trap air.
- Less surface area for gas exchange.
- Variation in V/Q

RESTRICTIVE LUNG DISEASES	
Reduced lung volumes (↓ FVC and TLC), PFTs show normal or ↑ FEV1/FVC. Short and shallow breaths.	
PNEUMOCONIOSIS (Caused by inhalation of INORGANIC DUST)	
Silicosis	<ul style="list-style-type: none"> ○ Affects upper lobes ○ Associated with glass manufacturers and stone cutters. Sandblasting. Mines ○ Macrophages respond to silica and release fibrogenic factors, leading to fibrosis. ○ It is thought that silica may disrupt phagolysosomes and impair macrophages, Increasing susceptibility to TB ○ “Eggshell” calcification of hilar lymph nodes on CXR with ground glass appearance.
Asbestosis	<ul style="list-style-type: none"> ○ Associated with shipbuilding, roofing Plumbing. Affects lower lobes ○ Characterized by ferruginous bodies (yellow-brown, rod-shaped bodies with clubbed Ends resembling dumbbells that stain positively with Prussian blue; found in alveolar Septum.) ○ “Ivory white, calcified, supradiaphragmatic and pleural plaques are pathognomonic of Asbestosis ○ Associated with incidence of lung cancer (bronchogenic carcinoma > mesothelioma) ○ Inc risk of caplan syndrome = pneumoconiosis + Rheumatoid arthritis + lung nodules. ○ Increased risk of pleural effusions also.
Coal Worker's Pneumoconiosis (CWP)	<ul style="list-style-type: none"> ○ Anthracois = Inhalation of carbon dust, Endemic in urban dwellers exposed to sooty air and causes no harm.

	<ul style="list-style-type: none"> ○ CWP: Affects upper lobes. Inhalation of coal dust, which contains both carbon and silica, Also known as black lung disease.
Berylliosis	<ul style="list-style-type: none"> ○ Affects upper lobes. Associated with exposure to beryllium in aerospace and manufacturing industries Granulomatous on histology and therefore occasionally responsive to steroids
ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)	
<ul style="list-style-type: none"> ○ It is an acute restrictive lung disease. ○ Triad of: Hypoxemia + dyspnea + bilateral lung opacities. ○ Also called non – cardiogenic pulmonary edema. ○ ↓ PaO₂/FiO₂ < 300 causes hypoxemia due to intrapulmonary shunting and diffusion defects. <p>Causes:</p> <ul style="list-style-type: none"> ❖ Direct injury → pneumoniae, aspiration, lung contusion, drowning and vape related injury. ❖ Indirect: sepsis, trauma, transfusion, pancreatitis, burns or drug overdose. <ul style="list-style-type: none"> ○ Pathogenesis involves diffuse alveolar damage leading to inc capillary permeability and leakage of protein – rich fluid into alveoli (Hyaline membrane formation) → non – cardiogenic pulmonary edema + normal pulmonary capillary wedge pressure (PCWP). ○ ARDS may be manifestation of severe acute resp syndrome (SARS). ○ SARS virus is a corona virus which damages pneumocytes especially type 2 and causes diffuse alveolar damage. ○ Manage by mechanical ventilation (↓ tidal volume), ↑ PEEP (keeps alveoli open during expiration) 	

ACUTE RESPIRATORY DISTRESS SYNDROME

+ ARDS

- ✓ **Pathology** —
- ✓ Alveoli fill with fluid.
- ✓ Acute onset of dyspnea, hypoxemia, & pulmonary infiltrates.
- ✓ **Consequences** —
- ✓ Reduced lung compliance, Increased pulmonary dead space, Inc. risk of pneumothorax & Pulmonary Hypertension
- ✓ 40% mortality rate
- ✓ **Treatment** —
- ✓ Address underlying causes
- ✓ Mechanical ventilation
 - Volutrauma (overdistention)
 - Alectrauma (alveolar strain)
 - Biotrauma (migration of pro-inflammatory molecules & pathogens).
- ✓ Fluid management to reduce L. atrial filling pressure (ex: diuretics); Neuromusc. blockade?

+ Newborn Respiratory Distress Syndrome

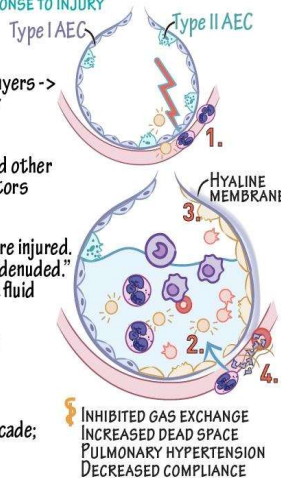
- ✓ Inadequate surfactant production by premature lungs; lungs collapse.

Pathophysiology

EXUDATIVE PHASE- INITIAL RESPONSE TO INJURY

Days 1-7

1. Inflammation damages endothelial & epithelial layers -> Increased permeability
2. Protein-rich fluid, activated neutrophils and other pro-inflammatory mediators fill the alveoli.
3. Alveolar epithelial cells are injured. Basement membrane is "denuded." Surfactant production & fluid resorption is inhibited. Hyaline membranes form (cellular debris, fibrin)
4. Endothelial damage triggers coagulation cascade; microthrombi can form.



Causes: Lung Injury

DIRECT

Pneumonia
Aspiration (gastric contents)
Pulm. contusion
Near drowning
Vaping (EVALI)

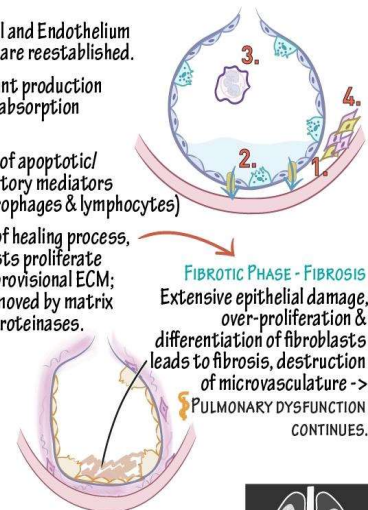
INDIRECT

Sepsis
Trauma
Transfusions
Pancreatitis
Drug reaction/ overdose

PROLIFERATIVE PHASE - BARRIER REPAIR & FLUID RESORPTION

Days 7-21

1. Epithelial and Endothelium barriers are reestablished.
2. Surfactant production & fluid reabsorption resume.
3. Removal of apoptotic/ inflammatory mediators (via macrophages & lymphocytes)
4. As part of healing process, Fibroblasts proliferate to form provisional ECM; Later removed by matrix metalloproteinases.

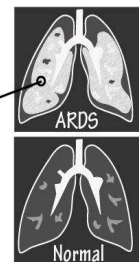


FIBROTIC PHASE - FIBROSIS
Extensive epithelial damage, over-proliferation & differentiation of fibroblasts leads to fibrosis, destruction of microvasculature -> PULMONARY DYSFUNCTION CONTINUES.

Diagnostic Criteria

BERLIN DEFINITION

Onset within 7 days of known clinical insult, or new/worsening symptoms during the last week.
Bilateral opacities "consistent with pulmonary edema"
Respiratory failure not fully explained by cardiac failure/fluid overload.
Acute hypoxemia (on a ventilator w/PEEP of ≥ 5 cm H₂O)
Mild: PaO₂/FiO₂ = 201-300 mmHg
Moderate: PaO₂/FiO₂ = 101-200 mmHg
Severe: PaO₂/FiO₂ = ≤ 100 mmHg



IDIOPATHIC PULMONARY FIBROSIS

Progressive fibrotic lung disease of unknown etiology. May involve multiple cycles of lung injury Inflammation, and fibrosis. Associated with cigarette smoking, environmental pollutants, genetic Defects.

Findings: progressive dyspnea fatigue non-productive cough crackles, clubbing

Imaging shows Peripheral reticular opacities with traction bronchiectasis +/- "honeycomb" appearance of lung (advanced disease)

Histologic pattern: usual interstitial pneumonia

Complications: pulmonary hypertension, respiratory failure, lung cancer, arrhythmias.

HYPERSENSITIVITY PNEUMONITIS

(Also known as extrinsic allergic alveolitis, Type III + IV HSR due to organic dust inhalation). Type are given below:

Type	Source	Agent involved
Farmer's lung	Mouldy hay	✓ <i>Saccharopolyspora rectivirgula</i> Microspolyspora faeni, Aspergillus fumigatus
Byssinosis	Textile industries	Cotton, flax/hemp dust
Begassosis	Sugarcane dust or residues	Sugar cane
Bird fancier's lungs	Bird excreta, protein, or feathers.	Avian serum proteins
Inhalation fever	AC contamination	Thermophilic actinomycetes
Malt workers	---	Aspergillus clavatus

GOOD PASTURE SYNDROME

Type II HSR due to Antibodies directed against glomerular membrane.

Presents with haematuria (glomerulonephritis) + hemoptysis (haemorrhagic pneumonitis)

EOSINOPHILIC GRANULOMATOSIS

Characteristics cytoplasmic inclusion resembling tennis racket – also called Birbeck granules.

SARCOIDOSIS

- Multisystem granulomatous disorder of unknown etiology that mostly affects lungs in middle age 20 – 40 yrs.
- Non – caseating granulomas > granuloma with asteroid bodies are typical features. Affects females > males.
- **Clinical features:**
- **Lungs:** 90% involvement, asymptomatic to chest pain, dyspnea, cough & bilateral hilar lymphadenopathy.
- **Common Extra pulmonary manifestation:**
- **Skin: Erythema nodosum** → painful purplish nodules especially on skin of shins. **Lupus pernio** – plaques on nose.
- **CVS:** heart blocks, arrhythmias, and sudden cardiac death
- **Eye:** anterior uveitis and sicca syndrome.
- Hepatosplenomegaly + peripheral lymphadenopathy.
- **Less common involvement** of CNS, Kidneys, and bones.
- Kidneys: renal stones and nephrocalcinosis. Bones: arthralgia. CNS: SOL brain and CN palsies.

Acute Sarcoid syndromes

1. **Lofgren's syndrome:** Fever, erythema nodosum, arthralgia and bilateral hilar lymphadenopathy
2. **Heerfordt – waldenstrom syndrome:** fever + Uveitis + parotid enlargement + facial palsy

Investigations:

- ❖ **Definitive Diagnosis:** Tissue biopsy/ Transbronchial lung biopsy, (lung, liver, lymph nodes, skin Nodules, or lacrimal glands) is diagnostic and shows non-caseating granuloma.
- ❖ **Serum Ca²⁺, 24 hr. Urinary Ca²** Increased due to increased formation of calcitriol
- ❖ **Elevated serum ACE** In about-60% (non-specific, non-sensitive)
- ❖ **CXR** is abnormal in 90%: (CXR changes in Sarcoidosis can be staged as follows:

Stage 0	Normal x – ray , no granulomas
Stage 1	Bilateral hilar lymphadenopathy (BHL)
Stage 2	BHL + Peripheral pulmonary infiltrates
Stage 3	Only pulmonary infiltrates
Stage 4	Pulmonary fibrosis

Inhalation Induced Lung Injury

- Complication of inhalation of noxious stimuli (eg. Smoke). Caused by heat, particulates (< 1 µm diameter), or irritants (eg. NH₃ → Chemical tracheobronchitis, edema Pneumonia, ARDS).
- Many patients present 2nd ry To burns, CO inhalation, cyanide poisoning Or arsenic poisoning
- Singed nasal hairs or soot In oropharynx common on exam.
- Bronchoscopy shows severe edema, congestion Of bronchus, and soot deposition.

LUNG CANCERS

Risk factors & Symptoms

Smoking (includes passive/2nd hand smokers also), Radon exposure, asbestos, radiations, genetic factors, occupational – Arsenic, Nickel, and heavy metal workers. Remember the sequence of risk factors for lung cancer as follows:

Smoking > Radon > Asbestos

- Keep in mind that Nickel causes Lung Cancer > Nose adenocarcinoma.
- Smoking causes Squamous cell lung cancer > Small cell lung cancer.

Presentation: cough, hemoptysis, wheeze, clubbing, coin lesion on CXR or non – calcified nodule on CT.

Classification of Lung cancers

- **Small cell Lung cancers**
- **Non – small cell lung cancer:** They include Squamous cell cancer, Adenocarcinoma, and large cell cancer.
- Adenosquamous, Anaplastic, sarcomatoid carcinomas and Carcinoma of undifferentiated type.
- **Adenocarcinoma** is more common in non – smokers and females, associated with EGFR mutation.
- Adenocarcinoma is the most common type of lung cancer.
- Squamous cell cancer and small cell lung cancer are central in origin while adenocarcinoma is peripheral in origin
- Carcinoid tumors have excellent prognosis. Present with flushing + wheeze + diarrhea. Chromogranin A +ve

Small cell or Oat cell cancer (Central)	<ul style="list-style-type: none"> ❖ Neoplasm of neuroendocrine kulchitsky cells (small blue cells), very aggressive. ❖ Amplification of L – Myc oncogene is common, early haematogenous spread. ❖ Treated by chemotherapy, amenable to surgical resection.
Squamous cell carcinoma (Central)	<ul style="list-style-type: none"> ❖ Most common in smokers. ❖ Keratin pearls with intercellular bridges on histology.
Adenocarcinoma (Peripheral)	<ul style="list-style-type: none"> ❖ Most common in lung cancer overall, more in females and non – smokers ❖ Amenable to EGFR tyrosine kinase inhibitors.
Large cell carcinoma (Peripheral)	<ul style="list-style-type: none"> ❖ Pleomorphic giant cells, may secrete HCG ❖ Highly anaplastic undifferentiated tumor, poor prognosis.

Complications & Paraneoplastic syndromes

- **Superior Vena Cava Syndrome:** Compression or invasion of the superior vena cava, resulting in Facial swelling and Cyanosis along with dilation of the veins of the head. Neck, and upper extremities
- **Pancoast tumor (Superior Sulcus tumor):** Involvement of the apex of the lung . often with Horner syndrome (ipsilateral ptosis Miosis, and anhidrosis), due to involvement of the cervical sympathetic plexus, Also Causes SVC syndrome, hoarseness (Recurrent Laryngeal Nerve Compression)

Paraneoplastic syndromes associated with lung cancers are:

- **Squamous cell cancer:** Hypercalcemia of malignancy due to PTHrp, pancoast syndrome in apical cancers.
- **Small cell cancer:** ↑ ACTH → Cushing syndrome, ↑ ADH → Syndrome of inappropriate ADH (SIADH) – hyponatraemia present, carcinoid syndrome and SVC syndrome
- Lambert Eaton myasthenic syndrome due to antibodies against pre – synaptic Ca⁺ channels.
- **Large cell cancer:** Gynaecomastia
- **Adenocarcinoma:** Hypertrophic osteoarthropathy, Trousseau syndrome → leads to marantic endocarditis

Metastasis

- ❖ **From Lung Cancer to Other Sites:** Adrenals. Brain. Bone (pathologic fracture). Liver (jaundice. Hepatomegaly)
- ❖ **To The Lung from Other Sites:** Most often from breast, colon, prostate, and bladder cancer

MESOTHELIOMA

- Malignancy of pleura linked to asbestosis, may result in hemorrhagic pleural effusions + pleural thickening.
- Tobacco smoking is not a risk factor.
- Histology may show Psammoma bodies.
- EM May show polygonal tumor cells with microvilli, Desmosomes and tonofilaments.
- Calretinin and cytokeratin.5/6 +ve in almost all Mesotheliomas.

LUNG CANCER, Part 1

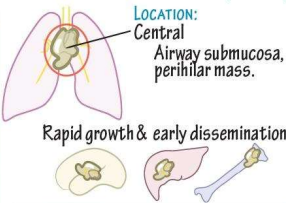
+ Lung Cancer

- ✓ Tumors from respiratory epithelium of bronchi, bronchioles, alveoli.
- ✓ Key cause of cancer deaths worldwide.
- ✓ Primary tumors can cause chest pain, cough, dyspnea, hemoptysis (late stage)
- ✓ Complications depend on location and/or cell type.
- ✓ Diagnosis of type includes histopathology and molecular analysis.
- ✓ Cigarette smoking (80-90%). Asbestos, radon, polycyclic aromatic hydrocarbons, metals
- ✓ Associated w/ several genetic changes (driver mutations, amplifications, translocations, deletions, insertions, etc.).

+ Pleural Mesothelioma

- ✓ Pleural cancer, most often caused by asbestos.
- ✓ Pleural thickening and effusions are common.
- ✓ Difficult to treat.

Small Cell Carcinoma (SCLC) ~15%



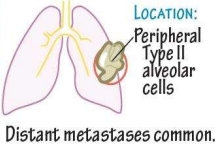
HISTOPATHOLOGY:
Small, spindle/round; high mitotic rate.
Scant cytoplasm; granular chromatin.
Necrosis is common.
Origins: Neuroendocrine cells (Kulchitsky cells) from basal bronchial epithelium.
Subtypes: Pure & Combined w/ large cells or NSCL cells

KEY POINTS:

Cigarette smokers (nearly all cases)
Genetics: MYC oncogene mutations, RB1 & TP53 inactivations.
Biomarkers: Neuron-specific enolase, Chromogranin A, Synaptophysin, CD56
Complications: SVC syndrome, SIADH, Cushing Disease, Lambert-Eaton synd.

Non-Small Cell Carcinoma (NSCLC) ~85%

Adenocarcinoma (~40%)



HISTOPATHOLOGY SUBTYPES:
Mucinous/Nonmucinous



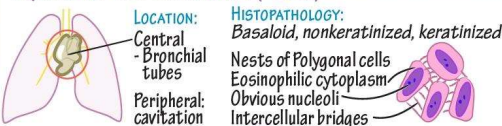
INVASIVENESS:

Preinvasive (lepidic)
AAH, AIS
Minimally invasive
Lepidic + other infiltrate myofibroblastic stroma.
Invasive (>5mm)
Mixed histopath.
Often Mucinous.

KEY POINTS:

Most common lung cancer overall.
Most common lung cancer in Women & Nonsmokers.
EGFR, KRAS, ALK, etc. mutations
Targeted therapies!

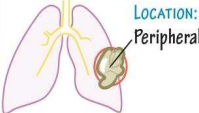
Squamous Cell Carcinoma (~30%)



KEY POINTS:

Strong assoc. w/smoking, TP53 & P-450 mutations.
Hypercalcemia (PTH-rp)
Weakness, nausea, vomiting, abdominal cramps, dehydration,

Large Cell Carcinoma (< 10%)



HISTOPATHOLOGY:
Poorly differentiated, large cells.

KEY POINTS:

Strong assoc. w/smoking. Several "subtypes" have been reclassified (ex: LCC no longer includes LC neuroendocrine carcinoma).

"Diagnosis of exclusion"

Only diagnose w/surgical resection. If cytology only: "non-small-cell lung carcinoma, not otherwise specified" (NSCL-NOS).

LUNG ABSCESS

- Localized collection of pus within parenchyma
- Caused by aspiration of oropharyngeal contents (especially in patients predisposed to loss of Consciousness [e.g., alcoholics, epileptics]) or bronchial obstruction (e.g cancer)
- Due to anaerobes (e.g **Bacteroides**, Fusobacterium, Peptostreptococcus) or S. Aureus.
- **Air-fluid levels often seen on CXR.**

NOTE:

Pneumoniae and TB are discussed in infectious disease & Microbiology section respectively.

PNEUMOTHORAX

- Accumulation of air in pleural space
- Unilateral chest pain and dyspnea, unilateral chest expansion
- **↓** tactile fremitus (only increased in consolidation e.g pneumonia), hyper resonance, Diminished breath sounds, all on the affected side.

Primary Spontaneous	Secondary spontaneous	Traumatic Pneumothorax	Tension pneumothorax
Due to rupture of apical blebs or cysts. Occurs most frequently in tall and thin young males .	Due to diseased lung (e.g bullae in emphysema, infections) Mechanical ventilation with use of high pressures causing barotrauma.	Caused by blunt (e.g rib fracture) or penetrating (e.g Gunshot) trauma	Air enters pleural space but cannot exit. Increasing trapped air → tension pneumothorax Trachea deviates away from affected lung

PLEURAL EFFUSION

Excess Accumulation of fluid between pleural layers causes restricted lung expansion during Inspiration Can be treated with thoracentesis to remove/reduce fluid.

Based on the Light Criteria**1. Exudative Fluid**

- pleural fluid protein/serum protein > 0.5
- pleural fluid LDH/serum LDH > 0.6, or pleural fluid LDH > 2/3 upper limit of normal serum LDH.

Exudate is Cloudy fluid (cellular), due to **malignancy, inflammation, infection** (Pneumonia) collagen Vascular disease). Trauma (Occurs in states of vascular permeability). Often needs to be drained due to risk of infection.

2. Transudative Fluid (Transudate)

- Clear fluid (hypo cellular.
- Due to hydrostatic pressure (e.g , HF, Na⁺ retention)
- low oncotic Pressure (nephrotic syndrome, cirrhosis)

Lymphatic: Also known as chylothorax, due to thoracic duct injury from trauma or malignancy

Milky- Appearing fluid, ↑ triglycerides

ATELECTASIS

- Alveolar collapse or lung collapse leading to loss of lung volume is called atelectasis. TYPES are as follows.

Obstructive Atelectasis	Compressive Atelectasis	Contraction (cicatrization) Atelectasis	Adhesive
airway obstruction prevents new air from reaching distal airways, old air is Resorbed (e.g, foreign body, mucous plug, tumor)	external compression on lung decreases lung volumes (e.g, space-occupying Lesion, pleural effusion)	Scarring of lung parenchyma that distorts alveoli (e.g, sarcoidosis)	Due to lack of surfactant (e.g, RDS in premature babies)

Digital Clubbing

- Increased angle between nail bed and nail plate (> 180°). Pathophysiology not well understood;
- In patients with intrapulmonary shunt, platelets and megakaryocytes become lodged in digital Vasculature – local release of PDGF and VEGF.
- Can be hereditary or acquired. **Not typically associated with COPD or asthma.** Causes include:
- Respiratory diseases (idiopathic pulmonary fibrosis, cystic fibrosis, **bronchiectasis, lung cancer**)
- Cardiovascular diseases (cyanotic congenital heart disease)
- infections (**lung abscess**, TB) and others (IBD) or malabsorption syndrome

Important Clinical (Physical) Findings In Lung Diseases					
Examination	Pleural effusion	Simple Pneumothorax	Tension Pneumothorax	Atelectasis	Consolidation
Breath sound	↓	↓	↓	↓	Bronchial breathing
Vocal fremitus	↓	↓	↓	↓	↑
Percussion	Stony Dull	Hyper resonant	Hyper resonant	Dull	Dull
Tracheal Deviation	Opposite side	None	Opposite side	Ipsilateral	None

Pulmonary Hypertension, DVT & Pulmonary Embolism

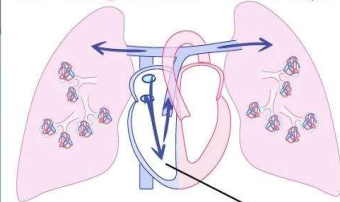
- 5 causes of Pulmonary HTN alongwith pathogenesis and features are explained below.
- Gold standard for DVT – Duplex scan.
- Investigation of choice for DVT – Doppler ultrasound.
- **D – dimers: high sensitivity in DVT and FDPs has: high specificity.**
- For DIC: D – dimers: high specificity and FDPs have: high sensitivity.
- **Investigation of choice in PE: CT – Pulmonary angiogram (CTPA) or Gallium scan**
- DVT involves commonly deep vein of legs (Popliteal vein – most common)
- **DVT causing embolism source is: Femoral vein**

PULMONARY HYPERTENSION

+ Key Points

- ✓ **Definition** —
- ✓ Increased pressure in pulmonary vasculature.
- ✓ MPAP ≥ 25 mmHg at rest
- ✓ Some argue > 20 mmHg
- ✓ **Symptoms** —
- ✓ Shortness of breath esp. on exertion
- ✓ **Consequences** —
- ✓ Right heart failure (cor pulmonale), arrhythmias, clots, bleeding into the lungs

Pulmonary Arterial Pressure (PAP)



Normal MPAP ~ 15 mmHg

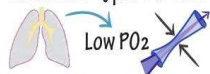
Groups of Pulmonary Hypertension

1. **PULMONARY ARTERIAL HYPERTENSION (PAH) $< 5\%$**
 - ✓ Causes vary: Idiopathic, hereditary (BMP2 gene), toxins, HIV, CTD.

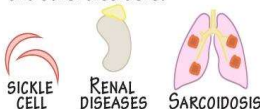
- ✓ Precapillary: PAWP ≤ 15 mmHg; Elevated PVR ≥ 3 WU

INFLAMMATION, FIBROSIS, THROMBOSIS, VASOCONSTRICTION

3. **PH DUE TO CHRONIC LUNG DISEASE/HYPOXIA $\sim 10\%$**
 - ✓ Causes: COPD, ILD, Obst. Sleep Apnea, etc. cause Hypoxic vasoconstriction



5. **PH DUE TO MISC./UNKNOWN CAUSES $\sim 15\%$**
 - ✓ Hematological, systemic, metabolic, and other disorders.



Left Heart Disease & PH

L. ATRIAL P \uparrow , PULMONARY PRESSURE \uparrow , LVEDP \uparrow

✓ "Reactive" PH can develop when HF causes arterial dysfunction, contributing to PH (mixed).

\uparrow Transpulm. gradient & Pulmonary Vasc. Resistance

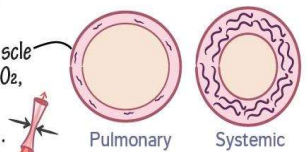
Pulmonary circulation = Low Pressure, Low Resistance, & High Compliance

✓ $PAP = (CO \times \text{Pulmonary Vascular Resistance}) + \text{Pulmonary Venous Pressure}$

- ✓ **PVR** = Low b/c vessels are short, wide, little muscle
- Modulators: Lung volume, perfusion pressure, O_2 , CO_2 , pH, etc.

- Hypoxia induces pulmonary vasoconstriction.

- ✓ **Compliance** = High b/c vessels are thin, little muscle tone.



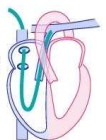
Diagnosis

DETERMINE PRESENCE, SEVERITY, AND CAUSE

- ✓ **Chest radiograph** = Enlarged pulmonary artery & pruning
- ✓ **Contrast Chest CT** = Thromboembolic PH (G4), LHF, ILD (G3)
- ✓ **Echocardiography, ECG, & Cardiac MRI** = Abnormal structure/function can indicate severity (RV), cause (LV)
- ✓ **Lung tests** = Spirometry, Diffusion capacity of CO_2

Definitive Test:

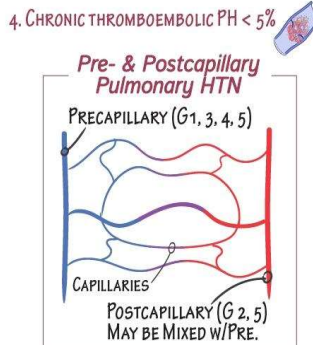
- ✓ **RH catheterization** = Measure pressure in RV and Pulm. artery.



Treatment

- ✓ Treat cause (Lung disease, LHF, etc.)
- ✓ O_2 , diuretics, digoxin, anti-coag, exercise
- ✓ Vasodilators are helpful for some (G1, PAH)

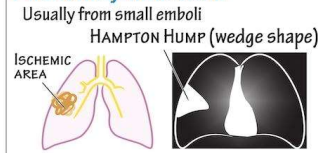
2. **PH DUE TO LEFT HEART DISEASE $\sim 70\%$**
 - ✓ Causes: Systolic/diastolic dysfunction, valvular disease, congenital disorders.
 - ✓ PAWP > 15 mmHg
 - ✓ PVR < 3 WU = Isolated Postcapillary
 - ✓ PVR ≥ 3 WU = Mixed ("Reactive")



PULMONARY EMBOLISM & DEEP VEIN THROMBOSIS

- + Pulmonary Embolism**
- ✓ Pathology —**
- ✓ Obstruction of pulmonary art.
 - ✓ Emboli are most often from DVT (calf/thigh/pelvis)
 - Deep vein thrombosis + Pulmonary embolism = Venous thromboembolism
 - ✓ Nonthrombotic sources
 - Air, fat, amniotic fluid, septic, foreign body, tumor.
 - ✓ PE Complications —
 - ✓ Pulmonary hypertension
 - ✓ Right heart failure
 - ✓ Pulmonary infarction
 - ✓ Treatments —
 - ✓ Supportive therapy
 - Oxygen, saline, vasopressors.
 - ✓ Anticoagulation
 - Acute: Heparin, Fondaparinux
 - Long term: Oral Anticoagulants
 - ✓ Embolectomy or clot dissolution

Pulmonary Infarction



Deep Vein Thrombosis

- ✓ Virchow Triad — Predisposing factors**

Endothelial injury

Fracture, surgery, trauma, previous DVT

Venous Stasis

Immobilty, Elevated CVP, Heart failure, Obesity

Hypercoagulation States

Pregnancy (+ IVC stasis)
Postpartum
Smoking (+endo. damage)
Cancer
Combined Hormonal Contraceptives
Hormonal Replacement Therapies
Coag. disorders

Symptoms

Swelling, tenderness, venous dilation

- ✓ Post thrombotic syndrome**
Chronic venous insufficiency

- ✓ DVT Diagnosis**

Wells Score for DVT

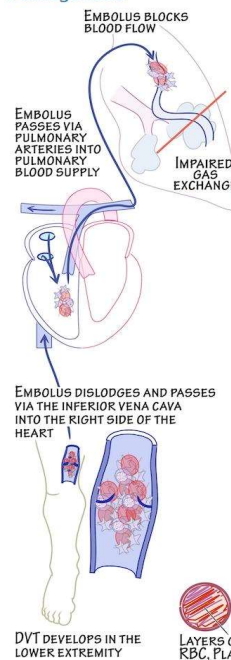
D-dimer:

- Used to rule out DVT when there is low probability

Imaging:

- Contrast venography
- Compression venous U/S (ultrasonography)

Pulmonary Embolism Pathogenesis —



Symptoms & Signs —

Dyspnea, Tachypnea, & Chest Pain
Hypoxia, V/Q mismatch, & Respiratory Alkalosis

Tachycardia & Right Heart Failure

Altered mental state (in elderly).



Classification —

By Risk:

High (massive), Intermediate, Low
Hemodynamic Instability vs. Stability

By Location:

Saddle, lobar, segmental, subsegmental



Pulmonary Embolism Diagnosis —

PE Wells Score > 4 means PE is likely.

D-dimer level is used to rule out PE when there is a low likelihood of PE. If > 500 ng/ml, additional PE testing is necessary.

Additional Tests:

V/Q scan is noninvasive

Chest CT w/ angiography

Chest X-Ray:

Possible atelectasis, Hampton hump (pulmonary infarction), Westermark sign (oligemia), Effusion.

ECG: Sinus tachycardia (S1Q3T3 sign is rare)

Lines of Zahn in thrombi formed premortem



SLEEP APNEA

- Repeated cessation of breathing > 10 seconds during sleep – disrupted sleep – daytime Somnolence.
Diagnosis confirmed by sleep study.
- Nocturnal hypoxia – systemic and pulmonary hypertension, arrhythmias (atrial fibrillation/flutter), sudden death.
- Hypoxia → EPO release → erythrocytosis.

Obstructive sleep apnea (OSA):

- Respiratory effort against airway obstruction. Pao₂ is usually normal during the day. Associated with Obesity, loud snoring, daytime sleepiness. Usually caused by excess Para pharyngeal/ oropharyngeal Tissue in adults, adenotonsillar hypertrophy in children. **It may lead to HTN, IHD, DM and fatigue.**
- Treatment: weight loss CPAP, dental Devices, hypoglossal nerve stimulation, upper airway surgery.

Central Sleep apnea:

- Impaired respiratory effort due to CNS injury/toxicity, Congestive HF, opioids. May be associated With Cheyne-Stokes respirations (oscillations between apnea and hyperpnea).
- Treatment: positive Airway pressure

Obesity Hypoventilation syndrome

- Also called Pickwickian syndrome. Obesity (BMI > 30 kg/m²) → hypoventilation
- Low Pao₂, during Waking hours (retention), low Pao₂ + high Pao₂ during sleep.
- Treatment: weight loss, positive airway Pressure.

CYSTIC FIBROSIS

- **Autosomal recessive** multisystem disease due to mutation of CFTR gene on chromosome 7.
- Disease involves exocrine glands (pancreas), respiratory system and GIT
- Respiratory symptoms include cough, sinusitis, recurrent chest infections, pneumoniae (by staph aureus)
- GIT symptoms include **chronic pancreatic insufficiency (80%)**, meconium ileus and rectal prolapse
- **Diagnosis** requires any of : Typical clinical features or History of sibling with CF or +ve new-born screening test.
Plus: **Sweat chloride test (> 60 mmol/L) – diagnostic**, CFTR gene mutation + Increased nasal potential difference.
- **Management:** Fat soluble vitamins (A , D, E, K) + pancreatic enzyme replacement + antibiotics + vaccination.
- Lung transplantation -- Definitive treatment

Pneumomediastinum

- Presence of gas (usually air) in the mediastinum. Can either be spontaneous (due to rupture of Pulmonary bleb) or 2" (trauma, iatrogenic, Boerhaave syndrome).
- Ruptured alveoli allow tracking of air into the mediastinum via peribronchial and perivascular sheaths
- Clinical features: chest pain, dyspnea, voice change, subcutaneous emphysema,
- **Hamman sign +ve: crepitus on cardiac auscultation**

Head & Neck Cancers:

- Mostly squamous cell carcinoma, Risk factors include tobacco, alcohol, HPV-16 (oropharyngeal) EBV (nasopharyngeal).
- **Field cancerization:** carcinogen damages wide mucosal area- multiple Tumors that develop independently after exposure
- Nasopharyngeal carcinoma may present with unilateral nasal obstruction, discharge, epistaxis, CN palsies.
- Eustachian tube obstruction may lead to otitis media +/- effusion, hearing loss.

Larynx Cancer:

- **Risk factors:** smoking, alcohol, coal dust, HPV, radiations, genetic,
- **Types:** Subglottic, glottic and supraglottic. Most common is supraglottic type. Mostly Squamous cell cancer occurs.
- **Presentation:** cough, hoarseness of voice, weight loss, hemoptysis, ringing in ears , feeling of lump
- **Investigations & Management:** laryngoscopy, biopsy, CT/MRI -- for staging.
- Treatment options are chemotherapy, radiotherapy, surgery, and immunotherapy.
- Subglottic cancers have worse prognosis.

Type 1 Respiratory Failure	Type 2 Respiratory Failure
Hypoxemia present no hypercapnia (normal CO ₂)	Hypoxemia (dec Blood O ₂) + Hypercapnia (inc. Blood CO ₂) PaO ₂ < 8KPa (< 60 mmHg) ; PaCO ₂ < 6KPa (< 45 mmHg). 1 KPa = 7.5 mmHg
<u>Examples:</u> <ul style="list-style-type: none"> ○ Pulmonary embolism ○ Pneumonia ○ ARDS ○ R to L shunt ○ pulmonary edema 	<u>Examples:</u> <ul style="list-style-type: none"> ○ COPD ○ asthma ○ GBS ○ ankylosing spondylitis. ○ Motor neuron disease.

PAST PAPER BCQs – ONE LINERS

1. In arterial blood, dissolved co ₂ (1.4 ml/100 ml) is more than the Dissolved oxygen (0.3 ml/100 ml) because = plasma solubility of co ₂ is 20 times greater than that of O ₂ (The plasma solubility of: CO > Co ₂ > Oxygen)
2. HB affinity of: CO > Oxygen > Co ₂
3. What changes occur at high altitude = Right Ventricular hypertrophy
4. T – configuration of Hb (tight) has low affinity for = O ₂
5. Single breath N ₂ test is used to measure = anatomical dead space
6. Diffusion capacity of O ₂ is measured by single breath test
7. Normal FEV ₁ /FVC = 0.8
8. Goblet cells present in = conducting zone
9. Half-life of Carboxy – Hb at 100% O ₂ = 40 – 80 minutes
10. Half-life of Carboxy Hb at room air = 4 – 6 Hrs and half life at hyperbaric O ₂ = 15 to 30 mins
11. Directly proportional for O ₂ diffusion is = alveolar surface area of capillary
12. VC less than 80% in = Restrictive lung disease
13. Alveoli don't collapse due to = surfactant
14. Tidal vol in baby is = 4 – 6 ml/kg
15. In old compliance of lung = increased
16. Alveolar ventilation = (VC – Dead space) × RR
17. During bronchoscopy first visualized structure = Upper lobe bronchus
18. Less in fetus than mother = PO ₂
19. No.of division of lower airways = 23
20. Hypoxia causes vasoconstriction in = Lungs only
21. Lipid bilayer is highly soluble for = CO ₂
22. After RTA a pt having Bicarb _s 16 , ODC Right shift due to = low PH (Metabolic acidosis due to low HCO ₃ ⁻¹)
23. Bradykinin released from lungs acts on = ductus arteriosus
24. Torr is a unit of = pressure
25. Change in volume per change in pressure = Compliance
26. Posture is maintained during exercise through = Proprioception
27. The effect of oxygenation on Carboxy – Hb is via = Le - chatelier
28. During hiking a person developed dyspnea and low PO ₂ the cause = Hypoxic hypoxia
29. Peripheral chemoreceptors respond especially to = low PO ₂ (Po ₂ < 60 mmHg)
30. During aging what remains same = TLC (VC increases) → read changes in elderly and pregnancy
31. During pregnancy the finding is = low PCO ₂ (due to hyperventilation)
32. Mixed blood source = Pulmonary artery
33. The vol remaining in lungs after normal expiration = FRC (read Volumes and capacities)
34. Lung expands due to = negative pressure
35. At high altitude, increasing alveolar ventilation raises Ph of Plasma because = It decreases pco ₂ in the alveoli (due to Hyperventilation → decreased alveolar and blood Pco ₂ → Resp alkalosis
36. Following cardiac changes occur during inspiration = A decrease in systemic arterial pressure Explanation: During inspiration, the intrapleural pressure decreases (more negative). This produces a suction force, thus pulling blood from systemic veins and left ventricle towards the heart. This increases cardiac output of the right heart and decreases cardiac output of the left heart. Due to ↓ output of the left heart, systemic B.P decreases by 10 mmHg.
37. Due to ↓ B.P, the baroreceptor reflex is activated which activates sympathetic system, resulting in ↑ heart rate
38. During expiration, the thoracic pressure increases → ↑ Venous return to the left heart → ↑ Left heart output → ↑ Systemic pressure → Baroreceptor reflex activates parasympathetic system → ↓ Heart rate
39. A patient suffering from chronic respiratory failure is = likely to have a raised calcium level
40. The positively charged Ca ⁺ and H ⁺ compete for binding with negatively charged proteins. In chronic respiratory failure, respiratory acidosis occurs due to accumulation of Co ₂ in the body, resulting in increased H ⁺ ions in the blood → More H ⁺ bind with proteins → So, less Ca ⁺ bind with proteins → ↑ Plasma levels of free ca ⁺
41. The most common physiologic cause of hypoxemia is = Ventilation perfusion inequality

42. Which of the following act as oxygen binding proteins in Skeletal muscle = Myoglobin
43. In case of Inspiration, chest expansion occurs due to: Decreased intrathoracic pressure.
44. During inspiration, diaphragm moves downward → Chest volume increases → Intrathoracic pressure (intrapleural pressure) decreases (pressure is inversely proportional to volume) → Air flows from outside atmosphere to alveoli (atmospheric pressure is zero and intrapleural pressure is less than zero; hence, air flows from higher to lower pressure) → chest expansion occurs.
45. Exchange of gases through lungs depends upon = Partial pressure difference of the gases + Surface area available for gas exchange + Diffusion distance + Solubility and molecular weight of the gases
46. Diffusion of gas across a membrane is inversely proportional to = molecular weight of the gas.
47. Factors that affect rate of diffusion through Respiratory membrane = pressure difference across the respiratory membrane
48. The most efficient gaseous exchange takes place in the = Alveoli
49. During the transport of oxygen in the arterial blood the Highest tension of oxygen (pO ₂) is seen in = Pulmonary capillaries
50. A 57-year-old clerk who is a chronic smoker presented with Cough and was cyanosed. The most likely findings will be = Increased concentration of deoxygenated Hb
51. Hypoxemia does not depend on = Hb
52. Pao ₂ does not depend upon HB concentration in the body (e.g, anemia, in which HB concentration is decreased, or Polycythemia, in which HB concentration is increased, does not affect Pao ₂ and hence, does not cause hypoxemia).
53. A patient was bed ridden developed DVT, and later complaint of chest pain and SOB. The finding = V/Q mis match
54. Decrease surfactant causes = patchy atelectasis
55. Which of the following decreases arterial O ₂ saturation without decreasing arterial O ₂ tension = Carbon monoxide poisoning
56. Partial pressure of oxygen in arterial blood depends on = Amount of oxygen in air
57. it's the dissolved oxygen only (and not the oxygen attached to HB) which exerts pressure.
58. At the end of expiration = Intra-pleural pressure is sub atmospheric
59. At the end of inspiration, the intra-pleural pressure is – 8, and at the end of expiration, the intra-pleural pressure is – 5. So, the intra-pleural pressure is always negative and less than atmospheric pressure.
60. Atmospheric pressure can be quoted as approximately = 1 bar or 760 mmHg
61. Normal quiet expiration is brought about by contraction/recoil of = Elastic tissue in thoracic and lung wall
62. Finding in a patient of drowning = Pulmonary Edema
63. Finding on ABGs early in drowning = Metabolic acidosis, late → Resp acidosis
64. Co ₂ transport is example of = negative feedback
65. Remember negative feedback in = CO ₂ transport, hormones regulation + homeostasis – control of internal environment. For + ve feedback → remember example of Childbirth and clotting mechanism of blood
66. A pt Hb = 14 g/dL, O ₂ content 20 mL, alveolar PO ₂ 40 and venous is 15 what type of hypoxia = Hypoxic hypoxia
67. A medical student, whose baseline alveolar PCO ₂ level was 40 mm Hg, begins to voluntarily hyperventilate for an experiment during his respiratory physiology laboratory. If his alveolar ventilation quadruples and his CO ₂ production remains constant, approximately what will be his alveolar PCO ₂ = 10 mm Hg
68. Explanation: When you hyperventilate, CO ₂ is blown off. The amount of CO ₂ blown off is inversely proportional to alveolar ventilation. This is shown by the alveolar ventilation equation: $VA = VCO_2 / PACO_2$,
69. Where VA = alveolar ventilation, VCO ₂ = CO ₂ production, PACO ₂ = alveolar PCO ₂
70. So, if VCO ₂ remains the same, and VA quadruples, PACO ₂ must decrease by 4-fold; 40 mm Hg decreases to 10 mm Hg.
71. The respiratory system undergoes changes in pregnancy the change causing distress in pregnant women is mostly = Dyspnea due to decreased paCO ₂ levels
72. A person having anemia the systemic arterial blood oxygen content is decreased. What will be its effect on alveolar ventilation = Increase
73. Copd patient o ₂ pressure at 10 cm of water by PEEP for 24 hrs would cause = Pneumothorax
74. If a person inhales 500 ml. Of air during each breath with respiratory rate 10 Breaths /min . Calculate the alveolar ventilation = 3500 ml/min
75. Explanation: Minute ventilation = RR x (TV - dead space) = 10 (500-150) = 3500 mL/min
76. During moderate exercise = Alveolar ventilation increases
77. Pt with septicaemia, on Ventilatory support. More and more Ventilatory pressure required to maintain ventilation x-ray shows opacities. What is mechanism = diffuse alveolar damage > intra alveolar neutrophilic exudate Scenario of ARDS.
78. What remains in lungs after maximum expiration = RV
79. A/a ratio is more than = 75% (0.75)

80. ODC shift to left = Haldane effect in lungs , Bohr effect → Right shift of ODC
81. Normal quiet inspiration = diaphragm and Normal expiration due to = passive recoil of lungs
82. Forced inspiration = external intercostal muscle
83. Forced expiration due to = internal intercostal muscle and abdominal muscles (rectus abdominus)
84. Accessory muscle of inspiration = SCM, Scalene muscles
85. Accessory muscle of expiration = Abdominal muscles
86. Venous drainage of lungs is via = Pulmonary vein
87. Serotonin and bradykinin both are inactivated in lungs while AT - 2 activated in lungs
88. I/v drug user with recent travel history presents with cough and SOB investigation reveal multiple cavity lesions in entire both lungs and nodular lesions The organism involved is = <i>S. Aureus</i>
89. What remains in lungs after expiration of tidal volume = FRC
90. Hering bruer reflex = to prevent overinflation of lungs, when stretch receptors of lungs are stimulated afferent go through vagus Nerve → inspiratory center in medulla inhibited + pneumotaxic center in pons activated
91. Apneustic center inhibited, inspiration ceases and expiration starts
92. vagus nerve nucleus ambiguus and dorsal motor nucleus also inhibited causing tachycardia
93. So Apneustic center for deep inspiration and Pneumotaxic center to stop breathing.
94. Fetus is in fear of respiratory distress, Best drug for lungs maturity = Hydrocortisone
95. Parasympathetic effect on lungs = inc restrictive work (due to bronchoconstriction).
96. What determines alveolar pressure of water = Ambient temperature (also humidity)
97. What determines water vapour pressure = Temperature of surrounding environment. (Both scenarios same) There are H ₂ O vapours in alveoli which contribute to alveolar pressure. Explanation: The alveolar pressure of water, or water vapour pressure, is determined by the temperature of the surrounding environment. It is a measure of the partial pressure of water vapour in the air within the alveoli of the lungs. As the temperature increases, the alveolar pressure of water also increases, and vice versa. This relationship is described by the concept of "saturation vapour pressure," which is the maximum water vapour pressure that the air can hold at a given temperature
98. Which anaesthetic is most resistant to metabolism = Halothane
99. Inspiratory ramp signals are produced from dorsal respiratory neurons. Their rate increases in response to impulses from = pneumotaxic centre in pons
100. Rate is increased by pneumotaxic centre (inhibitory centre that cut down the ramp signal leading to a faster rate of breathing).
101. Damage To Pneumotaxic Center = Deep Breathing (normally prevent excessive deep breathing)
102. Damage to Apneustic Center = Shallow Irregular Breathing (Normally promotes deep Breathing)
103. Transection above the level of pons = No effect on respiration
104. Transection at Mid-Pontine Level (pneumotaxic) With Vagi Cut = Apnoeisis
105. Transection at Ponto-Medullary Junction = Irregular Breathing
106. Transection Below Medulla = Stoppage Of Respiration.
107. Duration of inspiratory Ramp signals are controlled by pneumotaxic center which inhibit inspiratory signals From Apneustic center
108. Lung stretch receptors are activated By Over distention of lung which decrease respiratory rate by = Hering breuer reflex
109. Patient with anemia + dec PaO ₂ = Hypoxic hypoxia
110. High altitude results in = dec O ₂ affinity (Rt shift ODC – O ₂ unloading inc)
111. What happens to FRC in pregnancy = decreases
112. Tertiary or segmental bronchus aerates = Broncho pulmonary segment
113. Amount of CO ₂ dissolved in plasma at 45mmHg = 2.7%. At 40mmHg → 2.4%. 0.3% difference, hence 0.3ml CO ₂ is transported / 100 mL blood → 7% total
114. Receptors involved in cough after exposure to cold is = irritant receptors
115. Surfactant is produced by = type 2 pneumocytes
116. Peak expiratory flow measures = predicted value of FEV ₁ and assess large airways calibre
117. Central and peripheral chemoreceptors both respond well to = PCO ₂
118. During exercise = pulmonary vessel resistance decreases
119. IV lactic acid will stimulate = central chemoreceptors in medulla
120. In obstructive lung diseases what capacity increases = FRC

121. At apex of lungs = V/Q is high (apex of lungs → dead space) in zone 1 of lungs dead space is high
122. At high altitude inc breathing due to = Decreased arterial PO ₂
123. Hyperventilation occurs due to = dec PO ₂ (Because it leads to inc PCO ₂ which results in hyperventilation)
124. Cells present in inter alveolar septum = macrophages
125. Hypothermia shifts ODC to = Left shift ODC
126. Normal A – a gradient = 0.8
127. During Exercise RR is increased by Joint Proprioceptors > Peripheral Chemoreceptors.
128. Respiratory center present in = Medulla (or respiration is controlled by = Medulla)
129. What occurs in acclimatization at high altitude = inc in pulmonary ventilation
130. Extreme left shift of ODC seen in = CO poisoning
131. If carbon dioxide increases in the blood then respiratory rate will = increase
132. Vagus forms efferent pathway for = Hering reflex
133. Which group of Neurons, inactive normally are activated in medulla during increased breathing = Ventral group
134. Apneustic center for control of breathing present in = lower pons
135. Brain bridge reflex = it inc HR and Occulocardiac reflex → Dec HR
136. Hering breuer reflex → dec RR
137. In progressive shock finding will be = Met acidosis + Resp acidosis (mixed type)
138. Tb is transmitted by: inhaled aerosol
139. FRC is sum of = ERV + RV
140. Parameter to differentiate obstructive from restrictive lung diseases = FEV ₁ /FVC
141. Find O ₂ saturation of a person breathing in decompressed chamber of pressure 275 mmHg = 21%
142. Explanation: Normal Po ₂ in 1 atm (760 mmHg) = 160 mmHg. Here in scenario the pressure given is 1/3 rd of normal pressure so O ₂ pressure will also be 1/3 rd of normal. 160/3 = 53 approx.
143. O ₂ content of blood = PO ₂ /atm → 53/250 = 0.21 Multiply this to 100 for getting percentage → 21% approx.
144. Max diffusion capacity = CO ₂ and to measure diffusion capacity → CO is used
145. Majority of blood CO ₂ is carried in which form = HCO ₃ ⁻¹ 70%
146. V/Q ratio in embolism = Infinity
147. In airway obstruction V/Q is = below Normal ; for Shunt V/Q = 0
148. Function of dead space = air conditioning
149. PO ₂ In arterial blood is less than alveoli due to = Oxygen needs gradient to diffuse
150. In CO poisoning pt. present with dyspnea , SOB headache and hypercapnia. Finding will be = Normal PaO ₂
151. At height , suppose dead space is one third of VT. PCO ₂ of venous blood = 45 what will be EtCo ₂ / PeCO ₂ = 30 $VD = VT \times (PACO_2 - PECO_2) / PACO_2 \rightarrow VD/VT = PACO_2 - PECO_2 / PACO_2 \dots \text{suppose } peco_2 = x$ $150/500 = 45 - x / 45 \text{ Upon cross multiplying } \rightarrow 6750 = 500 (45 - x) \rightarrow 6750 = 22500 - 500x$ $6750 - 22500 = -500x \rightarrow 15750 = 500x \rightarrow x = 15750/500 \rightarrow 31.5 \text{ mmHg approx.}$ <p>The given options in exam was 30 , Closer to 31.</p>
152. ODC shifts to left in renal hypoxia leads to = Compensatory erythropoiesis
153. ODC in CN poisoning = Normal (PaO ₂ is also normal)
154. O ₂ 100% present in = L To R shunt
155. In exercise V/Q = 1
156. Blood flow to muscle maintained by = low pH (Rt shift)
157. Effect of anemia on alveolar ventilation = increased , alv ventilation dec by → Hering – beurer reflex
158. In obstructive lung disease = FEV ₁ /FVC is dec + FRC high
159. In restrictive lung diseases = elastic recoil increases + FRF dec + FEV ₁ /FVC same or inc.
160. Hypotension effect on dead space = increased
161. Bronchoconstriction effect on dead space = decreased
162. Dead space is unchanged in = shallow breathing
163. Chloride shift occurs via = Band 3
164. Venous blood have more = PCV > HCO ₃ (packed cell vol or Haematocrit)
165. RBC venous blood has more = Chloride
166. V/Q and arterial PO ₂ is highest at = Apex of lungs
167. V/Q and arterial PO ₂ lowest at base

168. Pulmonary blood flow and ventilation highest at = apex and both V & Q lowest at → base
169. Erythropoietin is produced by = Hypoxia and inhibited by = Theophylline
170. Atelectasis effect on dead space = Decreases
171. ETT effect on dead space = Inc Dead space
172. Pulmonary vasoconstriction is accentuated by = inc CO ₂
173. At 75% saturation O ₂ = 40 mmHg
174. P ₅₀ in right shift = 35 mmHg
175. Major difference b/w PO ₂ and PCO ₂ of arteries is present in = Aorta and Pulmonary artery
176. What happens to lung compliance in emphysema = increased
177. Regarding Anaemic hypoxia = NOT responsive to O ₂ therapy (as PaO ₂ is normal)
178. O ₂ delivery in 70kg man = 250 ml/min
179. Normal A – a gradient in = high altitude and hypoventilation
180. At rest lung volume is = FRC
181. At peak of inspiration lung vol = FRC + VT
182. FRC and FVC decreased in = Fibrosis
183. VD/VT ratio of PaO ₂ = 45 , PECO ₂ = 30 = 0.3 → by using formula $VD = VT \times (PACO_2 - PECO_2 / PACO_2)$
184. During spirometry, air inhaled maximum and then exhaled = Vital capacity
185. Lactic acid O ₂ debt = 8 Lit , Alactoid O ₂ debt = 3.5L
186. Diffusion Capacity of O ₂ = Dec in fibrosis
187. Respiration is unaffected by = Na ⁺ ions
188. Error in pulse oximeter reading in = Methemoglobinemia
189. Mucous glands absent in = terminal bronchioles
190. At atm 700 mmHg the pressure of O ₂ & N ₂ will be = PaO ₂ 147 & N ₂ 553
191. O ₂ pressure normal = 0.21 and N ₂ = 0.78. For O ₂ Multiply 0.21×700 = 147 , For N ₂ 0.78 × 700 = 553
192. Best defence in alveoli = alveolar Macrophages or dust cells
193. Clara cells present till = Terminal bronchioles
194. Goblet cells present in resp tract upto = Bronchi / Tertiary bronchus
195. Energy used in respiration = 2% (sometimes option of 5% given in exams) prefer 2% > 5%
196. Decreased Arterial oxygen tension in = dec atmospheric O ₂ (hypoxic hypoxia)
197. O ₂ sat. At sea level in healthy individual = 97%
198. Which volume Prevents lung collapse = residual Vol (RV – 1200 mL)
199. Normal insp capacity = 3300 – 3500 mL
200. Inc in PCO ₂ in non – anaesthetized patient in 1 st minute of apnea = 6 mmHg. After first minute rise in PCO ₂ = 3 mmHg. In anesthetized rise of Pco ₂ = 12 mmHg
201. Vascularity in lungs seen in = Canalicular stage
202. Find O ₂ content if Hb 10 g/dL , PaO ₂ = 60mmHg and O ₂ sat. 90% = 13. O ₂ content = Hb × 1.34 → 10 × 13.4 = 13.4
203. In airway obstruction, ventilation of alveoli is stopped what happens to PO ₂ In blood = equal to mixed venous blood in airway obstruction
204. Lungs bases have high V & Q due to = High Blood flow/ perfusion
205. In strenuous exercise inc ventilation due to = Collateral stimulation from higher centres
206. V/Q Lower than normal in = Shunt
207. Very small particles in resp system are removed via = Phagocytosis
208. Diameter of airways (bronchi) is under control of mainly = Sympathetic system
209. Normal respiratory drive is dependant on = PaCO ₂
210. Highest O ₂ tension is in = Pulmonary capillaries
211. Highest Saturation of O ₂ in = Umbilical vein
212. The respiratory zone for gas exchange extends beyond = Terminal bronchioles
213. Pulmonary artery pressure raised in = Moderate exercise
214. Hypoxemia in blood is sensed by = Carotid bodies
215. At normal conditions both are equal = Cardiac output & Venous return > Pulmonary blood flow & VR
216. At capnogram rise in baseline indicates = Rebreathing

217. Air humidity in OT = 55%
218. At 3000 ft barometric pressure = 226
219. For Shunt prefer $V/Q \rightarrow$ below normal $>$ Zero (Ref Guyton)
220. Regarding physiological dead space = equal to anatomical dead space normally (1:1 ratio normal)
221. Deficiency of surfactant leads to = inc surface tension + dec compliance
222. Hypoxic vasoconstriction in lungs due to = low PaO_2
223. Physiological dead space normally is = 150 mL
224. Hering – Breuer reflex leads to inhibition of = dorsal group neurons , prevents Overinflation of lungs
225. The PO_2 at which Hb is 50% saturated = 25 mmHg
226. Blood is warmed at 37°C for transfusion to cause = L to R shift
227. For forceful inspiration = Diaphragm + External ICM + SCM + Serratus anterior + Scalenii muscles
228. Vertical diameter inc by = Diaphragm , AP diameter inc by = External ICM
229. Low O_2 present in = pulmonary artery $>$ SVC $>$ Umbilical artery
230. Early stage of asthmatic attack with RR 25/min will show = Reduced arterial PCO_2
231. Neonate born premature develops RDS. What may be the finding = Collapse of small alveoli
232. When airway pressure is zero, the volume of combined resp system = FRC
233. Site of highest airway resistance = Medium size bronchioles $>$ Medium size bronchi
234. A 40 year old develops pulmonary embolism, completely blocks blood flow to left lung what will be finding = Alveolar Po_2 in left lung will be equal to Po_2 of inspired air
235. Hypoxemia produces hyperventilation via direct effect on = carotid + aortic body chemoreceptors
236. What Changes occur during strenuous exercise = Ventilation rate + O_2 consumption inc to same extent
237. If an area of lung is not ventilated due to bronchial obstruction, the pulmonary capillary blood flow serving that area will have PO_2 that is = equal to mixed venous oxygen.
238. In the transport of CO_2 from tissues to lungs, what occurs in venous blood = Conversion of CO_2 & H_2O to H and HCO_3^{-1} in RBCs
239. In which of following cause of hypoxia, inc A – a gradient + dec arterial PO_2 present = R to L shunt
240. A 30 year lady with pulmonary fibrosis, has PH 7.48, PaO_2 55 mmHg, $PaCO_2$ 32 mmHg. What explains the best regarding value of $PaCO_2$ = The dec PaO_2 stimulates peripheral chemoreceptors
241. At high altitude what happens to ODC = Right shift of ODC
242. PH of venous blood is slightly acidic than PH of arterial blood due to = H^+ generated from CO_2 + H_2O is buffered by deoxygenated Hb in venous blood.
243. In maximal expiration, the total volume expired = Vital capacity
244. The supplemental O_2 is helpful if V/Q defect is = Low V/Q
245. Largest A -a gradient seen in = Pulmonary fibrosis
246. A 48-year-old woman at sea level breaths A gas mixture containing 21% O_2 . She has the Following arterial blood gas values: Pao_2 -60 mm Hg, $Paco_2$ -45 mm Hg. Her measured $DLco$ is normal. Which of the
247. Following is the cause of her hypoxemia = Right-to-left shunt Explanation: Since the woman is hypoxemic at sea level and breathing a mixture Containing a normal % of O_2 , she cannot have normal lung function. Right-to-left shunt as the cause of the woman's Hypoxemia is further supported by calculating the A-a gradient as follows. $Pio_2 = (760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 0.21 = 150 \text{ mmHg}$, $PAO_2 = 150 \text{ mm Hg} - 45 \text{ mm Hg} / 0.8 = 94 \text{ mm Hg}$, A-a Gradient= $94 \text{ mm Hg} - 60 \text{ mm Hg} = 34 \text{ mm Hg}$, which is increased and consistent with R to L shunt.
248. A 57-year-old man at sea level breaths a mixture containing 21% O_2 . He has the Following arterial blood gas values: $PaO_2 = 60$ mm Hg, $PaCo_2$ 70 mm Hg. Which of the following is the cause of his Hypoxemia = Hypoventilation
249. Respiratory zone consists of = Respiratory bronchioles, alveolar ducts and alveoli..
250. Mucus secretion are swept out of lungs toward mouth by which cells = Ciliated columnar cells
251. Pulmonary surfactant contains = Dipalmitoyl phosphatidylcholine
252. Aspirated peanut at supine position reaches = Sup portion of right inf lobe
253. Aorta at T12 Other components are Thoracic duct and Azygous vein
254. Phrenic nerve root value = C3,4,5
255. Kallikrein activates = Bradykinin
256. Surfactants deficit in which disease = Neonatal respiratory distress syndrome
257. Vital capacity = $TV + IRV + ERV$

258. Which part of lung has largest contribution of functional dead space = Apex of healthy lung
259. Relaxed form of HB has high affinity for O ₂
260. Methemoglobinemia can be treated with = methylene blue + Vit C
261. Foetal dissociation curve is shifted to = left shift
262. Oxygen HB dissociation curve is sigmoid due to = Positive cooperatively
263. Normal pulmonary artery pressure = 10/4 mmHg
264. Cyanosis result when deoxyhaemoglobin HB reaches = > 5 mmHg
265. V/Q=0 what does it means = Airway obstruction (shunt)
266. CO ₂ is transported in forms = bicarbonate, carbamino hemoglobin, dissolved
267. Bohr effect seen in = peripheral tissues
268. Chronic hypoxia pulmonary vasoconstriction results in = RVH
269. Pulmonary embolism symptoms = Chest pain, tachypnea and dyspnea
270. Amniotic fluid emboli can lead to = DIC
271. Barrel shape chest seen in = Emphysema
272. Test for asthma = Methacholine challenge
273. Bilateral hilar lymphadenopathy and non caseating granuloma = Sarcoidosis
274. Which affects lower lobes = Asbestosis
275. In neonatal respiratory distress syndrome therapeutic supplemental O ₂ can result in = Retinopathy of prematurity
276. NRDS Persistent Low O ₂ tension, risk of = PDA
277. Curschmann's spiral seen in = Asthma
278. Asbestosis associated with = Bronchogenic carcinoma > pleural mesothelioma
279. Surfactant is made by cells? And mostly abundant after week of gestation?? Type II Pneumocytes and 35 th week of gestation
280. Treatment of sleep apnea = Weight loss, CPAP, surgery
281. Dull percussion note = Pleural effusion
282. Coin lesion on X-ray film = Granuloma
283. Absence of cartilage differentiates resp zone from = Trachea
284. Lung carcinoma associated with smoking = Squamous cell carcinoma
285. Spontaneous pneumothorax tracheal deviation which side = Towards side of lesion
286. Carcinoid tumors secretes = Serotonin
287. Salt and pepper histological feature seen in = Small cell lung carcinoma
288. Horner syndrome = Ptosis, miosis and anhidrosis
289. Most common cause of lung abscess = Staph aureus
290. Farmer disease shows which type of hypersensitivity reaction = Mixed type II/III
291. Facial plethora seen in = SVC obstruction
292. In pneumothorax = dec tactile fremitus
293. Spontaneous pneumothorax most commonly occurs because of = Rupture of apical bleb
294. Name 1 st generation H ₁ blockers = Diphenhydramine, dimenhydrinate, chlorpheniramine
295. Theophylline causes bronchodilators by = Inhibits phosphodiesterase
296. Mast cell stabilizers = Cromolyn
297. Drug of pulmonary hypertension = Bosentan
298. Dextromethorphan act on which receptors = NMDA glutamergic receptors
299. Name the transcription factor that induces production of TN alpha? NFkB
300. Lymphatic pleural effusion also called? Chylothorax
301. Psammoma bodies seen in which lung disease? Mesothelioma
302. Most aggressive lung carcinoma? Small cell lung carcinoma
303. Sleep apnea breathing stops for how much time? 10 secs
304. Risk factor for neonatal respiratory distress syndrome?? Prematurity, maternal diabetes, cesarean section
305. egg cell calcification of hilar lymph nodes? Silicosis
306. Hypertrophic osteoarthropathy associated with which lung carcinoma? Adenocarcinoma of lung
307. Drugs causing restrictive lung disease? Busulfan, bleomycin and amiodarone .
308. What sign is present in DVT? And how we check it? Homan sign, dorsiflexion of foot

309. Primary pulmonary hypertension is due to inactivation of which gene? BMPR2 gene
310. 1gm HB binds with = 1.34 ml O ₂
311. Pain from the diaphragm can be referred to ? Shoulder
312. In perfusion limited ... Diffusion can be increased only if increases = Blood flow
313. Common source of pulmonary embolism is = Femoral vein, whereas common source of DVT = Popliteal vein.
314. Diffuse lung fibrosis on CXR without fever or cough, the cause is = Inorganic dust
315. What happens to diffusion capacity of O ₂ in lung fibrosis = decreases
316. A patient with lung fibrosis has SOB and dyspnea. The cause is = dec diffusion capacity of O ₂ .
317. A 20 yr. non – smoker having fever for 1 month with cough + hemoptysis, on CXR Coin lesion is seen in upper lobe. It is linked to = Granuloma (T.B). Granuloma was given in options in exam instead of Tb.
318. Remember the most common cause of granuloma in young & adults is Tb whereas in old age it is related to lung cancer.
319. To confirm diagnosis of lobar pneumoniae the investigation to be done is = Sputum culture.
320. A Girl has bronchial obstruction, but alveoli do not collapse and still aerated by bronchus due to = Alveolar pore or pore of Kohn.
321. A 35 yr. Old previously normal lady started having dyspnea, dry cough, and fever 02 months back, recovered for 01 month when she went on vacations. She again developed symptoms after coming back to her canaries. CXR shows multiple nodular lesions in all lung zones. The mechanism of her symptoms is. = Antigen – antibody mediated reaction. (Scenario of Hypersensitivity pneumonitis)
322. Type of cells involved in sarcoidosis = T cells.
323. Indication for ETT = Short Neck.
324. Finding in kyphoscoliosis on PFTs = decreased vital capacity.
325. Pulmonary vasoconstriction is due to = Hypoxia (low PaO ₂). Remember : Low alveolar PaO ₂ > low systemic O ₂ .
326. Smoking related emphysema affects = Centrilobar or Centriacinar zone of lung.
327. Regarding alveoli true is = surfactant avoid collapse of alveoli.
328. The cause of farmer's lung is = Grain dust or Organic dust.
329. Which capacity increases in Obstructive lung diseases = FRC. (Also TLC)
330. What happens to RV in Obstructive diseases = Increases
331. Asbestosis is related to = malignancy.
332. A Man died after RTA, on autopsy black lymph nodes and black lungs due to = Anthracosis.
333. A HTN + DM lady developed dyspnea + hemoptysis 10 days after surgery. The cause = Pulmonary embolism.
334. Bronchogenic cancer metastasizes commonly to which gland = Adrenal gland.
335. Cause of interstitial lung disease = Inorganic dust.
336. Regarding pulmonary Tb, occurs in = Posterior part of upper lobe.
337. In weather changes and asthmatics having cough, receptors involved are = Nociceptors.
338. Low grade fever + cough + night sweats = Tb.
339. Definitive diagnosis of pneumonia requires = Sputum culture.
340. A man having TB diagnosed with retropharyngeal abscess. The structure it invades first = Prevertebral sheath.
341. Paraneoplastic syndrome is caused by = Small cell lung carcinoma.
342. A 50 yr. Male Presented with dec Oxygenation + Co ₂ retention. On call house officer performs X ray and lungs came out to be hyperinflated. Likely diagnosis is = Emphysema (obstructive pattern)
343. A female having RTA presented with BP = 80/40 and Pulse 140/m, she collapses, on autopsy macrophages and hyaline membrane seen on alveolar lining. The cause of death = diffuse alveolar damage. (Scenario of ARDS).
344. Patient has numbness at ulnar border of hands with facial congestion. Biopsy of lungs show Small cell carcinoma. What will be raised in SCLC = ACTH (Cushing syndrome, not cushing disease)
345. A 43 year male working in a sandblasting/ mine factory presented with cough + fever + hilar lymphadenopathy. The reason behind is = Silicosis (silicosis induced Tb).
346. The diagnosis is Tb, but the cause is silicosis.
347. Carbon laden macrophages develop in which disease = Anthracosis.
348. A pt. Of lung cancer presented with inc. Po ₄ in urine, inc. Ca in blood and raised PTHrp. The cause is = Squamous cell CA Lung.
349. Trachea is part of = Conducting zone of resp tract.
350. A male develops dyspnea 8 hrs after reaching to 14000 ft. in siachin. The cause = Pulmonary edema
351. Findings of chronic bronchitis = Reid index > 50 %.
352. History of fever, weight loss + granulomatous lesion on nose . The diagnosis = Leprosy. (Mycobacterium leprae – acid fast intracellular)

353. A 30 yr. old farmer contacted a disease from sheep and cattle. The skin lesion is black and ulcerated. Most likely cause is = Anthrax (a type of Zoonosis, use Ciprofloxacin, most common form is cutaneous anthrax in 70% of cases).
354. Difference b/w sarcoidosis & Tb is = bilateral hilar lymphadenopathy in sarcoidosis.
355. Schaumann bodies seen in = Sarcoidosis. (Ferruginous bodies in asbestosis).
356. Male working in construction factory presented with pleural plaques. The cause is = asbestosis.
357. A child with ARDS was given surfactant, the mechanism of action of surfactant = dec alveolar surface tension.
358. A female pt. With SOB, O/E basal crepts + pedal edema. The diagnosis is = Congestive HF.
359. A 50 yr. Male presented with bilateral leg swelling + pleural effusion. He is afebrile without any other symptoms. The labs are: CK 145, LDH 750, AST 270, ALT 240. Likely diagnosis is = Recurrent thromboembolism.
360. Pulmonary embolism leading to shock and death caused by = Thrombo-embolism.
361. In pulmonary embolism, alveolar PAO ₂ is equal to = Po ₂ in inspired air. (PAO ₂ = PiO ₂)
362. Regarding pulmonary embolism, correct is = alveolar PaO ₂ increases (because it gets equal to PiO ₂).
363. Vital capacity less than 80% present in which disease pattern = Restrictive lung diseases.
364. A pt. Had cough for 04 months with hemoptysis. On CXR Right Lung has 6cm hilar mass. Sputum cytology shows pleomorphic cells with scanty cytoplasm. The cause is = Radon exposure.
365. Scenario of lung cancer – no history of smoking given, the 2 nd leading cause is Radon gas.
366. COPD is diagnosed when FEV ₁ is = less than 0.8 (< 80%)
367. Asthma effects mostly = Medium size bronchioles.
368. Surfactant deficiency may cause = patchy atelectasis.
369. Hypercalcemia in squamous cell carcinoma is due to = Parathyroid hormone related peptide (PTHrp).
370. A patient working in a demolishing company develops SOB and dyspnea. CXR shows bilateral diffuse interstitial fibrosis. On biopsy of lung, iron staining of cells was +ve. The likely diagnosis = Asbestosis.
371. A patient working in cotton industry has risk of developing = Byssinosis. (Begassosis with sugarcane dust)
372. 7 yr. Old boy with dyspnea, fever 101 F°, RR 22/min, no history of cough/hemoptysis, sputum shows no growth on culture, ANA is -ve, on X ray lower lobe infiltrates + hilar lymphadenopathy. Diagnosis = LL lobar Pneumonia.
373. A 43 yr. Male presents with cough, fever for 04 months, cervical lymphadenopathy and non – healing ulcer on tongue. Histology shows granuloma with caseous necrosis. On CXR, Hilar lymph sign normal. The suitable diagnosis = Histoplasmosis. (Normal hilar lymph sign).
374. Remember : non healing tongue ulcer is seen in both Tb + histoplasmosis. The main difference is of hilar lymph sign. If +ve hilar lymph sign → Tb, if normal hilar lymph sign on chest x ray → Histoplasmosis)
375. A patient presented with dry cough, dyspnea and SOB. On CXR bilateral hilar lymphadenopathy. The diagnosis is = Non – caseating granuloma > Granuloma with asteroid. (Scenario of Sarcoidosis)
376. Regarding primary Tb true is = Gohn complex. (Primary Tb involves Lower lobe + Gohn complex present).
377. Cavitation is seen in which Tb = secondary Tb
378. A 70 yr. Old male c/o fever, cough, weight loss, hemoptysis, patches in lungs on CXR, on histology epithelioid cells present. Next best step is = AFB (to confirm diagnosis of Tb as the scenario relates to Tb)
379. A smoker presented with cough. On biopsy of alveoli, the finding may be = squamous metaplasia.
380. What increases in asthma = IgE
381. In chronic long – standing asthma, most likely change = increased lymphocytic response to mitogens.
382. A Premature infant developed RDS, what will be the finding in lungs = Decreased lamellar bodies in type 2 pneumocytes. (Surfactant is synthesized by these)
383. What happens to lung compliance in old age = increases. (Also RV, V/Q mismatch, A – a gradient raises)
384. Kartegener's syndrome involves = dynein arm (defect of dynein arm)
385. A 40 yr. Male develops developed lung abscess after eating street food due to = Direct extension from Liver.
386. Aspiration in upright posture lodges contents into = Right lower lobe - posterior zone.
387. Foreign body in supine goes to which area = Apical segment of Right lower lobe.
388. A pt. Presented with C/o cough, dyspnea and SOB. On CXR bilateral hilar lymphadenopathy. Biopsy shows granuloma with caseous necrosis. The likely cause is = Tuberculosis.
389. A male working in digging deep earth crust is at risk of = Silicosis.
390. LS ratio of amniotic fluid represents the function of = Fetal lungs.
391. Transudative fluid has = low cell count
392. Test sensitive for asthma = FEV ₁ /FVC.
393. In patient of COPD (emphysema), what is the finding on ABGs = Rise in plasma CO ₂ – respiratory acidosis.
394. Lung pressure volumes in emphysema show = increased lung volume – Right shift of loop.
395. Where pleural fluid tends to accumulate in excess = Costodiaphragmatic recess.

396.Regarding O2 therapy in anaemic hypoxia = it is Not responsive to oxygen. (Because PaO2 is normal)
397.A child having chronic cough was given ATT but did not resolve. On exam : clubbing, low weight, and pallor +ve. CXR shows Tram track sign. Most likely diagnosis = Bronchiectasis.
398.A 62 yr. Male smoker with cough, wheeze, dyspnea and 7cm hilar mass. The cause is = Smoking (Lung cancer).
399.Chronic smokers with hoarseness of voice and lymph nodes palpable in neck. likely cause is = Larynx cancer.
400.Chronic smoker + progressive dysphagia + palpable neck lymph nodes. The likely cause = CA Esophagus.
401.Prefer larynx cancer if Hoarseness present and Esophageal cancer in case of progressive dysphagia/dysphagia.
402.Alveolar macrophages are called = Dust cells.
403.A 70 yr. Male known case of blood dyscrasias, presented with sudden SOB, dyspnea. On Echo Pulmonary HTN was diagnosed. The possible cause = Repeated pulmonary emboli.
404.A known case of cystic fibrosis presented with pneumonia (pseudomonas +ve). The other finding may be = Bronchiectasis.
405.Mode of spread of TB = Aerosolized air droplets.
406.24 yr. old male with recurrent chest infections + chronic diarrhea + bronchiectasis. What test is most suitable for diagnosis = Sweat Chloride test. (A case of cystic fibrosis)
407.Farmer with chest pain + left sided lung calcification. The cause = Aspergillosis.
408.Commonest type of Lung CA = Adenocarcinoma.
409.Asbestosis may cause = Bronchogenic cancer (keep in mind, Lung Ca > Mesothelioma in asbestosis).
410.Diagnostic test for leprosy = Nasal scraping
411.Cause of angiosarcoma in plastic factory worker = Vinyl chloride (PVC)
412.Smoker + plastic factory worker. The possibility of which cancer is higher = Lung cancer.
413.Angiosarcoma in farmer. The cause is = Arsenic.
414.Peri hilar lymphadenopathy + epithelioid cells = TB
415.Man working at ship industry is at risk of developing = asbestosis → Bronchogenic carcinoma.
416.Cell of atopic asthma are = Mast cells (prefer Mast cell > Basophils > Eosinophils)
417.Following sudden relief in ARDS, A pt. May develop = Apnea (due to raised PaO2)
418.DLCO decreases in = lung fibrosis
419.What is the cause of increased activity of neutrophil elastase = Nicotine.
420.AARDS is linked to = Prematurity.
421.A male 30 yr. Old diagnosed with alpha 1 antitrypsin deficiency. Which part of respiratory tract would be most affected = Alveolar duct.
422.A 4 yr. Old child having cough and mucous, on CXR hyperinflated lungs and eosinophilia on CBC. The diagnosis may be = Asthma
423.Destruction of alveolar walls with decreased elastic recoil in a smoker = Emphysema.
424.A 25 yr. Mother presented with respiratory distress foetus should be given = Betamethasone (To inc. fetal lung maturity – IV betamethasone is given to mother).
425.Histological diagnostic feature of chronic bronchitis = Hypertrophy + Hyperplasia of mucous glands in airways.
426.Stony dull percussion note seen in = Pleural effusion.
427.In pneumothorax percussion note is = Hyper resonant.
428.Type 1 RF can't occur in = Drug overdose.
429.Pneumonia causes which type of RF = Type 1 respiratory failure (Type 1 RF)
430.A 50 yr. old male underwent cardiac transplantation 04 weeks ago, now complaint of cough, fever for 05 days. On CXR -- consolidation of Right Lower lobe, On CT brain – multiple brain abscesses. He was given antibiotics, but no improvement seen. Upon gram staining + culture – normal flora found. The likely cause is = Nocardia. (it may cause multiple brain abscesses, treat with Sulfonamides).
431.On biopsy of a lymph node, granuloma with caseous necrosis found, for diagnosing TB what is the next step = Demonstration of AFB.
432.A bird keeper developed cough and flu like illness. Multiple infiltrates on CXR. Cause = Chlamydia psittacosis
433. Histoplasmosis involves which organ mostly = Reticuloendothelial system.
434.After Head injury, a patient presented with pattern of breathing having increased respiration and decreased respiration. Rapid breathing followed by decreased breathing and then apnoea. This type of breathing is called = Cheyne stroke breathing.
435.End expiratory volumes will be raised in = COPD (volumes increased – air trapped).
436.After inhaling dust, a male develops cough, lacrimation, and wheeze. The type of HSR is = Type 1 HSR.
437.What happens to FEV1 in asthma = decreases.
438.CXR of a pt. Shows bilateral hilar lymphadenopathy. Biopsy shows granulomatous necrosis of salivary glands. The diagnosis is = Sarcoidosis.

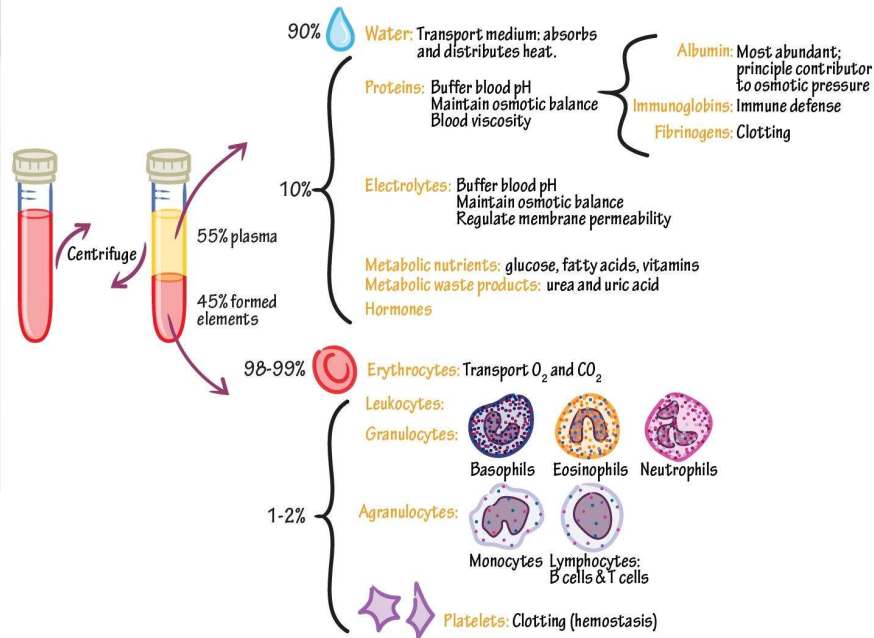
439. Fever + weight loss + bilateral hilar lymphadenopathy + tongue ulcer + caseous necrosis = TB
440. Regarding bronchial asthma, the probable finding is = FEV1/FVC < 65% (ideally less than 80%)
441. Small cell carcinoma is associated with = Cushing syndrome.
442. What will not be present in lung hamartoma = cartilage in lesion area. (As it is well defined lesion with nodules)
443. Increased vasculogenesis in lungs seen in which stage = Canalicular stage.
444. Antibodies against Ca ⁺ channels in = Lambert eaten syndrome.
445. A 16 yr. Old girl having SOB, Dyspnea, inc. RR, Auscultation and sputum results are normal. On CXR hilar lymphadenopathy on left side and nodular lesion on left middle lobe. The cause = Hypersensitivity pneumonitis.
446. Thymoma is linked to myasthenia and = Pure red cell aplasia.
447. A female having mass in periphery of lung = Adenocarcinoma.
448. A common skin finding in sarcoidosis = Erythema nodosum
449. A 7 Yr. Boy c/o SOB, dyspnea, hilar lymphadenopathy + 1.5 cm nodule in left middle lobe of lung. On CXR, On auscultation chest clear, gallop rhythm present but no murmur found. On CT Chest no mass found, sputum cytology is negative and all labs are optimal. The diagnosis might be = Carcinoid syndrome.
450. Alpha 1 antitrypsin deficiency is = autosomal recessive.
451. A 26 yr. Gardner having cough with chest pain occasionally. On CXR – Round calcified mass seen in right lung field. The cause is = Aspergillus (in gardeners + farmers).
452. On biopsy TB granuloma feature is = Caseating granuloma.
453. Most imp cells for diagnosis of granuloma are = Epithelioid cells.
454. A Pt. Presented with weak muscles with no improvement on giving neostigmine. Autoantibodies against voltage Ca ⁺ channels found. The diagnosis is = Lambert eaten syndrome.
455. A pt. Has lower resp tract infection for 02 weeks. What will be damaged in respiratory tree = Cilia.
456. Fibrovascular and mesothelial tissue seen under microscope = Lung.
457. In pneumothorax what happens = Lung collapse inward and chest wall springs outward.
458. Vasodilation by CO ₂ is maximum in = Brain.
459. Plasma protein = does not bind with oxygen
460. During exercise, blood flow increases in = Zone II + Zone III of lungs.
461. Rate of respiration controlled by = PCO ₂ .
462. Effect of inspiration on lung compliance = Increases.
463. COPD with SOB + respiratory acidosis predisposes to = Hyperkalemia.
464. Lung cancer having fungiform growth = Squamous cell cancer.
465. RA + Lung nodules + pneumoconiosis = Caplan syndrome.
466. What acts on neutrophil elastase = Nicotine.
467. Difference between neoplasm and granuloma = Rapid inc. In size.
468. Gardner with Right lower lobe lesion after pricked by a thorn while plucking roses = Sporothrix (sporotrichosis).
469. At FRC = chest wall expands and lungs recoil.
470. In Cheyne stoke's breathing = Tidal Vol. Increases and then gradually Dec.
471. Effect of Obesity on FRC = Decreases.
472. Interleukin that inhibits eosinophils apoptosis, playing role in asthma = IL – 5 .
473. In asthma always test antibodies against = aspergillosis
474. Test for aspergillosis = Glactomann
475. A pt. Of lung cancer has dilute urine. The cause = SIADH.
476. In pulmonary infarction what type of hypoxia seen = Stagnant hypoxia.
477. Hyperoxia is NOT seen in = Anemia.
478. Infertility + bronchiectasis + situs inversus = Kartegener's syndrome.
479. Infertility in kartagener syndrome due to = Immotile sperms > azoospermia.
480. What is not true about cystic fibrosis = 90% pt. Have both pulmonary + pancreatic disease.
481. An Obese lady postpartum, having chest pain, SOB, dyspnea, hemoptysis, low grade fever due to = Lung infarction.
482. A feature of SVC syndrome is = Facial congestion.
483. Atmospheric pressure = 1 bar or 760 mmHg
484. Air required for embolism = 100 cc.
485. Partial pressure of O ₂ at sea level = 80 – 100 mmHg.
486. Conc. Of normal air in middle air = N ₂ 83%, O ₂ 9%, CO ₂ 6%.
487. TORCH may cause congenital anomalies except = pneumonia.
488. Common cold is mostly caused by = adenoviruses

489. Acute epiglottitis X ray finding = Thumb sign
490. Acute laryngotracheobronchitis (croup) → steeple sign on X ray.
491. Chronic rhino sinusitis is frequently associated with = nasal polyps
492. Most common nasal tumor is = SCC
493. Lesion of vocal cords associated with heavy smoking = Singer nodule.
494. Most common malignant tumor of larynx = Squamous cell carcinoma.
495. Glottic cancers arise from true vocal cords and are most common vocal cord tumor.
496. Homozygous state of alpha 1 anti-trypsin (piZZ) associated with = pan acinar emphysema + hepatic cirrhosis.
497. Bronchiectasis involves = lower lobes commonly
498. Cause of primary Pulm HTN = Idiopathic
499. Most common cause of secondary pulmonary HTN is = COPD
500. Complication of Pulm HTN = Rt vent hypertrophy.
501. Growth along preexisting structures (Lepidic growth pattern) is seen in = Bronchoalveolar carcinoma.
502. A 2yr. Old girl having fever, hoarseness, seal – bark like cough, stridor. Her mother gives history of runny nose and sore throat in child. Most likely cause = Virus.
503. Hypercalcemia, hypergammaglobulinemia and inc. ACE activity is seen in = sarcoidosis.
504. A man died of asthma, at autopsy most likely finding is = bronchial smooth muscle hypertrophy + proliferation of eosinophils.
505. Elevated titres of cold agglutinins seen in = mycoplasma pneumoniae
506. Feature specific to secondary TB = Cavitation.
507. A 60 yr. Old male presented with restrictive lung disease. She describes aggressive disease course with rapid onset of SOB in past year. On lung biopsy, patchy process characterized by temporally heterogeneous areas of fibrosis present. What is expected clinical course = Poor Prognosis with development of honeycomb lung and death in 5 years. (A case of idiopathic pulmonary fibrosis/Usual interstitial pneumoniae)
508. A female non-smoker presented with tumor comprised of poorly formed glands. The most likely finding may be = positive for EGFR mutation (a case of lung CA)

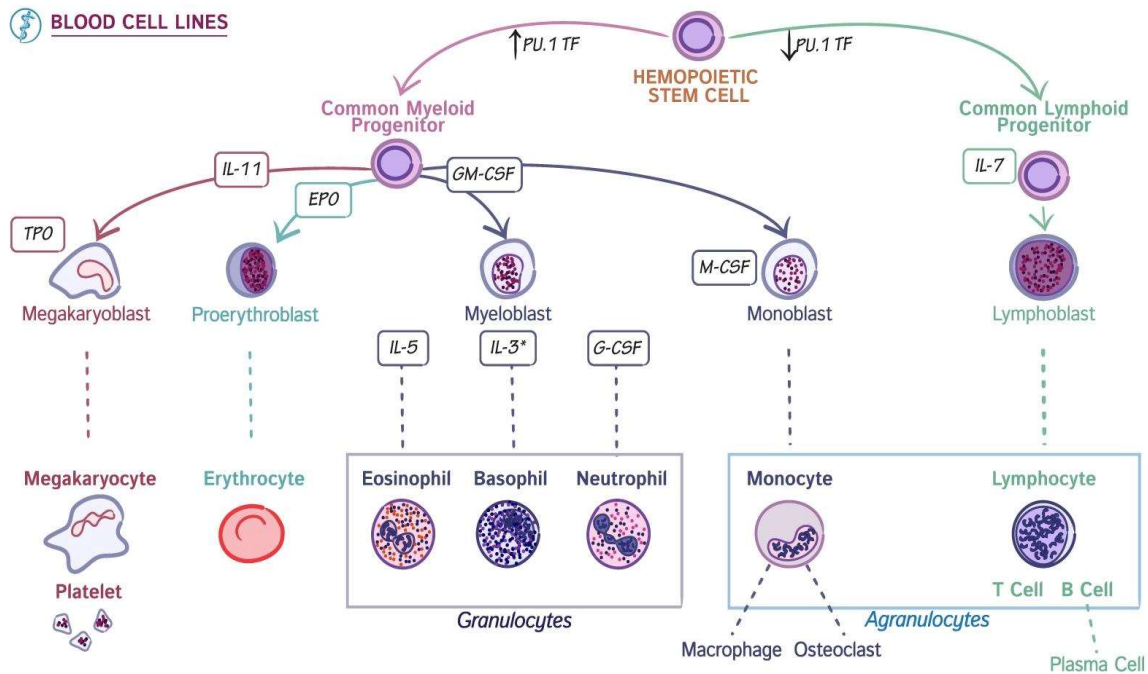
HEMATOLOGY & ONCOLOGY**HEMATOPOIESIS**

BLOOD COMPOSITION AND FUNCTION

- ✓ Blood: connective tissue suspended in plasma
- + Key Components**
- ✓ Blood Plasma —
 - ✓ Water
 - ✓ Proteins
 - ✓ Electrolytes
 - ✓ Metabolic nutrients and waste
 - ✓ Hormones
- ✓ Formed Elements —
 - ✓ Erythrocytes
 - ✓ Leukocytes
 - ✓ Platelets
- § Clinical Correlations**
- ✓ Deep Venous Thrombosis (DVT) —
The clumping of blood fragments in veins, caused by failure of adequate movement
- ✓ Hemophilia —
Genetic mutation causes deficiency in clotting factor

**Remember:**

- **Common Myeloid lineage** gives rise to → Erythrocytes, Megakaryocytes, myeloblasts → granulocytes (N, E & B) + Monocyte.
- **Common lymphoid progenitor** gives rise to Lymphocytes (agranulocytes) + Natural killer cells.
- So, lymphocytes share a different origin than other cells.
- **Diseases affecting myeloid lineage will not necessarily disturb lymphocytes** and will affect RBCs, PLT & Granulocytes.
- For example, in acute myeloid leukemia: whole myeloid lineage (RBCs, PLT & Granulocytes) is disturbed leading to pancytopenia.



PU.1 TF* = Pioneer Transcription factor 1.

ERYTHROPOIESIS	
Stage of Erythropoiesis	Important event
Proerythroblast	Synthesis of Hb starts (not appears)
Early normoblast (Basophilic erythroblast)	Nucleoli disappear. Ongoing Hb synthesis.
Intermediate normoblast (Polychromatophilic erythroblast)	Hemoglobin starts to appear .
Late normoblast (Orthochromatic erythroblast)	Nucleus disappear, maximum hemoglobin synthesis here.
Reticulocyte (Polychromatophilic erythroblast)	Reticulum is formed, cells enter blood. Maximum Hb concentration.
Mature RBC	Reticulum disappears, cells attain biconcave shape of diameter 7.5-8 um.
Ribosomes = Basophilic (Blue), Haemoglobin = Acidophilic (Pink)	
Characteristics of RBCs	
<ul style="list-style-type: none"> Carry O₂ to tissues and CO₂ to lungs. Anucleate, lack organelles, anaerobic glycolysis occurs (Embden pathway) biconcave with large Surface area-to-volume ratio for rapid gas Exchange. Life span of ~120 days in healthy Adults; 60-90 days in neonates. Source of Energy is glucose (90% used in glycolysis, 10% Used in HMP shunt). Membranes contain Cl/HCO₃⁻¹ antiporter, which allow RBCs to Export HCO₃ and transport CO, from the Periphery to the lungs for elimination Erythrocytosis = Polycythemia = ↑ Haematocrit Anisocytosis = varying sizes & Poikilocytosis = varying shapes Reticulocyte = immature RBC; reflects Erythroid proliferation. Bluish colour (polychromasia) on Wright-Giemsa Stain of reticulocytes represents residual Ribosomal RNA. 	

Fetal Erythropoiesis & Hemoglobin Development

Fetal erythropoiesis occurs in:

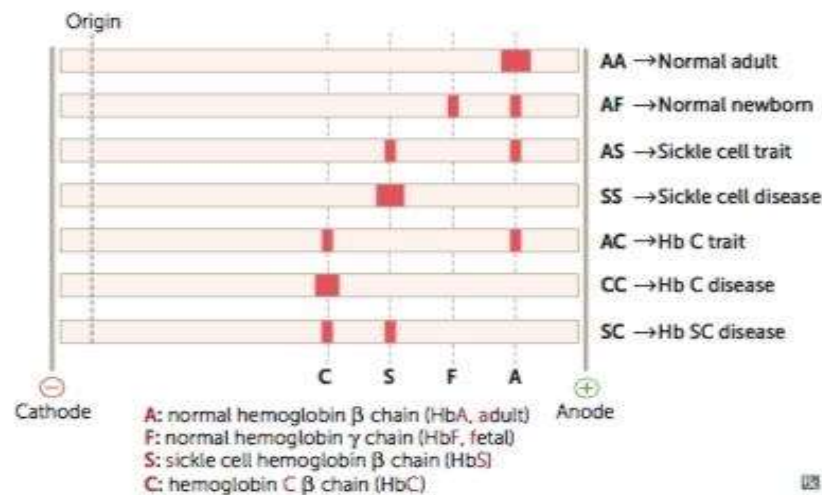
1. Yolk sac (3-8 weeks)
 2. **Liver** (6 weeks-birth) – main role.
 3. Spleen (10-28 weeks)
 4. Bone marrow (18 weeks to adult)
- Embryonic globins: 2 zeta + 2 epsilon chains
 - Fetal hemoglobin (HbF) = $\alpha_2\gamma_2$ (2 alpha + 2 gamma) – higher O₂ affinity due to less 2,3 – BPG binding
 - Adult hemoglobin (HbA₁) = $\alpha_2\beta_2$ (2 alpha + 2 beta)
 - HbA₂ (2 alpha + 2 delta chains) is a form of adult hemoglobin present in small amounts.

Hb – Electrophoresis (Mnemonics: A – Fsc)

On a gel, hemoglobin migrates from the Negatively charged cathode to the positively charged anode.

HbA migrates the farthest, followed by HbF, HbS, and HbC.

This is because the missense mutations in HbS and HbC replace glutamic acid (-ve) with valine (neutral) and lysine (+ve), respectively, making HbC and HbS more positively charged than HbA



RBC MORPHOLOGY	RBC INCLUSIONS
Acanthocytes/Spur cells: projections of varying size at irregular intervals, seen in: Abetalipoproteinemia, Liver disease, Vit E deficiency	Bone Marrow: <ul style="list-style-type: none"> • Iron Granules: require Prussian blue for visualizing. • Present in sideroblastic anemia (Lead poisoning)
Echinocytes: smaller and uniform projection at regular intervals, seen in CKD/ESRD, pyruvate kinase def.	Peripheral Smear
Dacryocytes: Tear shaped RBCs in bone marrow infiltration e.g myelofibrosis (BCQ)	<ol style="list-style-type: none"> 1. Heinz bodies: contain iron so they require crystal violet to be visualized. Formed due to denatured and precipitated Hb. A feature of G6PD deficiency anemia. 2. Howell Jolly bodies: basophilic nuclear remnants (no iron) usually removed by splenic macrophages. Associated with asplenia e.g sickle cell disease/ splenectomy. 3. Basophilic stippling: ribosomal precipitates (don't contain iron) present in sideroblastic anemia (lead poisoning) and rarely thalassemia.
Schistocytes: Fragmented RBCs/helmet cells. Seen in: DIC, TTP, HUS, HELLP syndrome, heart valve prosthesis.	
Spherocytes: small spherical cells without central pallor. Dec surface area to vol. Ratio Seen in Hereditary spherocytosis, autoimmune hemolytic anemia.	
Elliptocytes: mutation in genes for spectrin e.g hereditary Elliptocytosis.	
Degmacytes/Bite cells: due to removal of Heinz bodies by spleen e.g in G6PD deficiency.	
Target cells: ↑ surface area/volume ratio. Seen in Thalassemia, HbC disease and asplenia.	

Pencil cells: present in iron deficiency anemia.

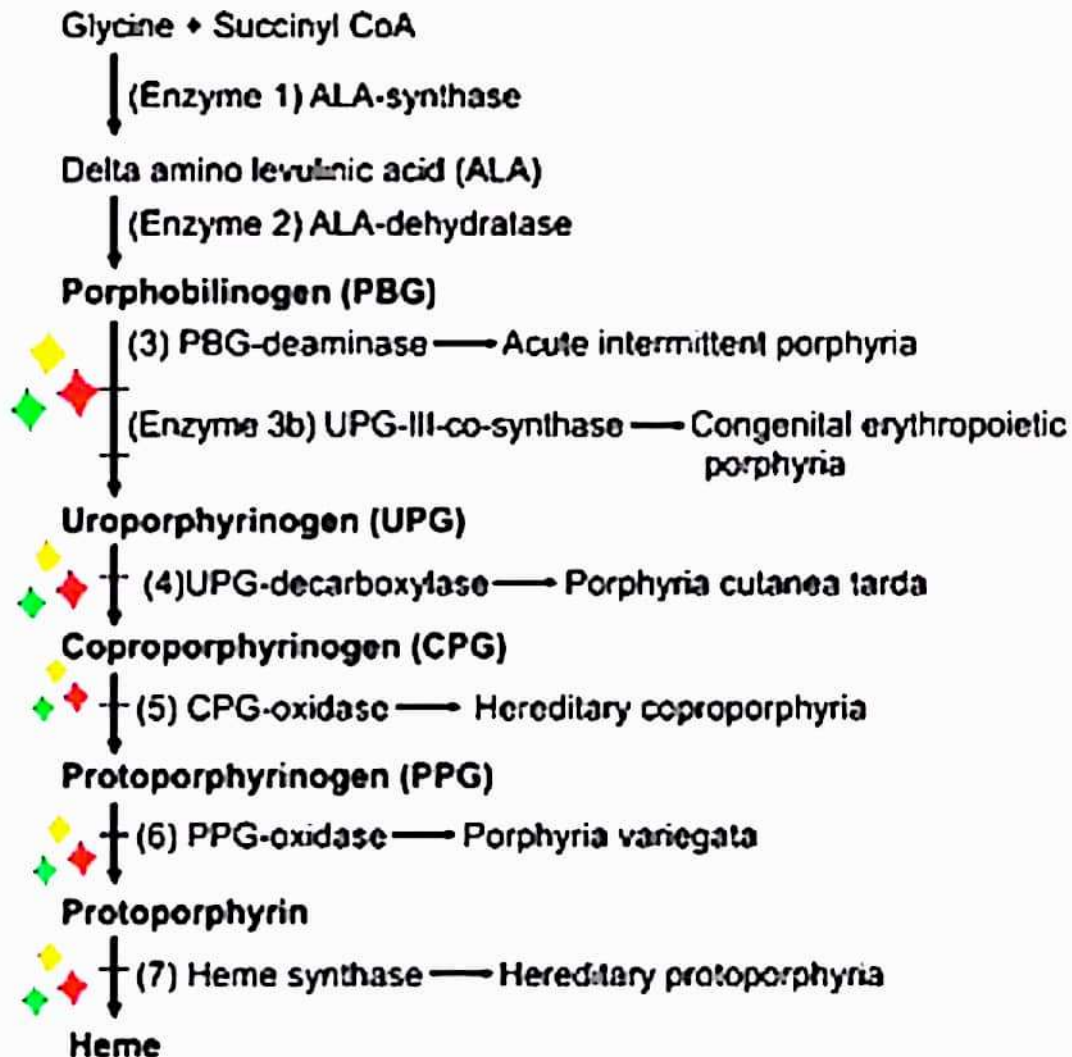
Sickle cells: sickle shaped due to hypoxia, acidosis or high altitude in sickle cell anemia.

Macro – ovalocytes : Megaloblastic anemia (B12/folate deficiency)

4. **Peppenheimer bodies:** Basophilic iron containing granules in sideroblastic anemia.

HEME SYNTHESIS & DISORDERS OF HEME SYNTHESIS (PORPHYRIAS)

- Heme synthesis mainly occurs in mitochondria from precursors Succinyl CoA + glycine. Porphyrins are conditions of heme synthesis, may be acquired/hereditary, leading to accumulations of heme precursors
- Most common porphyria is porphyria catenea tarda associated with Hep C & Alcohol
- Symptoms common to porphyria are Abdominal pain, photosensitivity and neuropsychiatric symptoms.



LEUKOPOIESIS

Hematopoietic stem cells (HSCs) → Myeloblasts → Promyelocyte → Myelocyte → Metamyelocyte → Band cells → Neutro/Eosino/Basophils.

Primary granules/Azuropophilic granules appear in Promyelocytic stage

Secondary granules appear first appear in Myelocyte stage and present in Metamyelocyte, band cells and neutrophils stage.

Characteristics of Cell Type		Abnormalities	
Neutrophils <ul style="list-style-type: none">50 – 70% of differential leukocyte count (DLC) Absolute value = 3000 – 6000 (varies)Phagocytic , Multilobed (1 – 4), stain pinkacute inflammatory cells.spend 6 hr in circulation before being removed by spleen. In tissues, half life is 3 to 4 days. Primary Azurophilic granules (lysosomes) contain: Myeloperoxidase, proteases, acid phosphatase. Secondary/Specific fine granules contain: Leukocyte alkaline phosphatase (LAP), Lysozyme, Lactoferrin and collagenases. <ul style="list-style-type: none">LAP Score increases in myeloid reaction like infection/ inflammation and dec. In CMLHypersegmented neutrophils (6+ lobed nuclei) seen in Megaloblastic anemia (B12/Folic acid deficiency)		Left shift: a state of inc. Myeloid proliferation. inc. Neutrophil precursor e.g (band cells) seen in peripheral blood e.g inflammation, infection/ CML. Leukoerythroblastic reaction = Left shift + immature RBCs Seen in bone marrow infiltration → myelofibrosis or Metastasis	
		Neutrophilia Inc. Neutrophils Seen in: <ul style="list-style-type: none">Bacterial infectionacute inflammationAspleniasteroids therapystress, exerciseITP and hemolytic anemia.	Neutropenia Dec. Neutrophils count less than 1500 cell/mm in: <ul style="list-style-type: none">sepsis, post infectionChemotherapyviral infections, malaria, leukemiaVit B12 def.
Lymphocytes + Natural killer cells <ul style="list-style-type: none">20 – 40 % of DLC. Count = 1500 – 2700Agranulocytes (lack granules), pale nucleusB lymphocytes: 20% of lymphocytes, mediate humoral immunity, produce memory B cells & Plasma cells. Plasma cells produce antibodies. Plasma cells have clock face chromatin, eccentric nucleus, abundant RER, well developed Golgi app.T lymphocytes are 80%, mediate cell mediated immunity. Involved in autoimmune diseases, graft rejection.NK cells are part of innate immunity. They are anti tumor and kill virus infected cells (not affected, but infected)		Lymphocytosis Seen in: <ul style="list-style-type: none">Viral, parasitic, and fungal infectionsRheumatoid arthritisLeukemiaLymphomaThymomaPost splenectomyCardiac emergenciesMost abundant cells in chronic inflammation are lymphocytes.	Lymphopenia Absolute neutrophil count less than 1500 cells/mm3 Less than 3000cells/mm3 in children. Seen in: <ul style="list-style-type: none">HIV, SCIDSLEDigeorge syndromeSteroids excesssepsisRadiationspost-Operative states
Eosinophils <ul style="list-style-type: none">2 – 4% of DLC, 150 – 450 Cell countBilobed – spectacle shaped nucleusProduce Major basic protein – anti parasitic.Eosinophil cationic protein + eosinophil peroxidase.		Eosinophilia Parasitic infestation Asthma, allergies Chronic adrenal insufficiency (Addison’s) Hodgkin lymphoma	Eosinopenia Absolute count < 30 cells. Cushing syndrome Corticosteroids therapy
Monocytes <ul style="list-style-type: none">2 – 6 % in DLC , 200 – 600 CellsFound in blood till 24 hrs.Differentiate into macrophages in tissue.Large kidney shaped nucleus- frosted glass cytoplasmMonocytosis is seen in Tb, brucellosis, fungal infection, Listeria, leukemia, lymphoma, IBD, sarcoidosis, cancers.		Macrophages Major phagocytic/scavenger in tissue Whereas neutrophils are phagocytic in blood. Activated by gamma interferon. Most imp cells in chronic inflammation. They are named according to location: Kupffer cell in liver, histiocytes in skin, mesangial cells in kidney. Can function as APC via MHC – II They fuse to form giant cells	

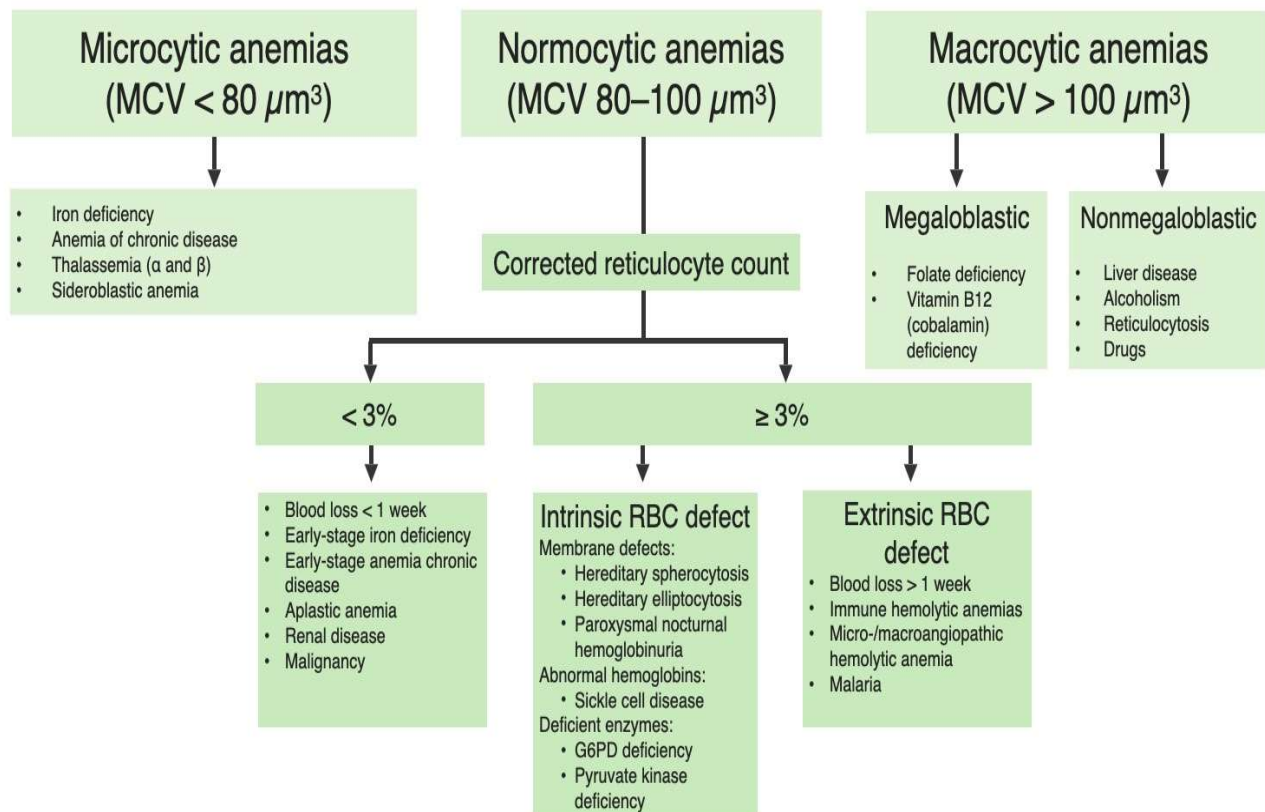
Basophils	Effect of Corticosteroids on WBCs
0 – 1 %, not present in blood normally. Contain dense basophilic granules that provide Heparin + histamine. Mediate allergic reaction igE is found on surface of Mast cells > Basophils.	Neutrophilia + Eosinopenia + Lymphopenia. Impair the migration of neutrophils via dec expression of Integrins, sequester eosinophils in lymph nodes + cause apoptosis of Lymphocytes (effective in blood cancers).

ANEMIAS

Decreased Hb with respect to age and sex of individual.

Classification Of Anemia on The Bases of MCV

- Morphological classification of anemia is done based on MCV as follows:
 - Microcytic: MCV less than 80 (Mnemonics: TAILS as given in table above)
 - Normocytic: MCV is equal to 80-100
 - Macrocytic: MCV greater than 100
- Mean corpuscular volume (MCV): it is the average volume of red blood cell. Normal value = 80-100 fL/ μm^3
- Mean corpuscular Hemoglobin (MCH) Normal value=27-33pg: it refers to the average mass Of Hb per RBC
- These tell us of Normo-chromic, Hypo-chromic or Hyper-chromic anemia



MICROCYTIC ANEMIA

(MCV < 80 fl) Mnemonics: TAILS

Thalassemia, Anemia of Chronic disease, Iron deficiency anemia, Lead poisoning and Sideroblastic anemia

Iron Deficiency Anemia

- Iron deficiency anemia is hypochromic Microcytic anemia
- Most common overall anemia, most common nutritional deficiency worldwide.
- Anemia is due to decreases iron due to chronic bleeding (e.g, GI loss, menorrhagia), malnutrition, absorption disorders, GI Surgery (e.g, gastrectomy), or high demand (e.g, pregnancy) ↓ final step in heme synthesis.
- Phytates, Tannates, phosphate, oxalate and carbonate all these have negative influence on iron Absorption.
- Vitamin-C, citrate and glucose help To convert ferric iron (Fe3) to ferrous iron (Fe2), this Reduced (Fe2+), directly reabsorbed in the duodenum.
- Intestinal absorption of iron mainly occurs in ferrous form, which found most abundant in meat.
- Plant contains the ferric form of iron. Methemoglobin: Hb -M bind with the ferric form of iron
- Iron stored in form of ferritin and transported in form of transferrin
- This is the common cause of anemia in pregnancy after Physiological anemia of pregnancy (not true anemia)

Symptoms: fatigue, conjunctival pallor, pica (persistent craving and compulsive eating of Non-food substances), spoon nails (koilonychia). May manifest as glossitis, cheilosis, Plummer-Vinson syndrome (triad of iron deficiency anemia, Esophageal webs, and dysphagia)

Labs: ↓ iron+ low MCV + low MCH + Low MCHC + low ferritin (most sensitive test) and low reticulocyte index.

↑ TIBC, + free erythrocyte protoporphyrin + RDW. (raised Platelets also by unknown mechanism)

Microcytosis and Hypochromasia (inc. central pallor) and Pencil cells on peripheral smear.

IRON

- Iron is mainly in hemoglobin (65%), 4% occur in Myoglobin, 10% of dietary iron is absorbed (in duodenum)
- Iron stored in female: 2 gm and Iron stored in males: 6 gram. Total body iron storage: 4gm
- The daily loss of iron: In male =1mg (into faeces), Female: 2mg (into faeces and menstrual blood)
- Iron stored in parenchymal tissue in the soluble form ferritin. Insoluble form of iron is hemosiderin
- The main regulator of Iron absorption is Hepcidin → A protein formed by the liver
- **Iron homeostasis is via ferritin, maintained by Hepcidin, controlled by transferrin.**
- **Hemopexin binds heme** and controls release of Fe into circulation and **heptoglobin binds Hemoglobin** released.
- **Transferrin** transports iron in blood. Ferritin is primary iron storage protein in body.
- **TIBC** indirectly measures transferrin.
- **Iron tablet taken on an preferably with citrus juice** > empty stomach which helps the body absorb them better
- The best indicator of serum iron store is serum ferritin (also best diagnostic in pregnancy).
- Iron demand in pregnancy: 800mg
- Ferrous fumarate has approximately 33% elemental iron. Ferrous sulphate has 20% elemental Iron. Ferrous gluconate has 12% elemental iron.
- Iron poisoning causes death due to free radicals formation + peroxidation of lipid membranes.
- Acute toxicity causes GI bleeding, Met acidosis and chronic may cause cirrhosis, cardiomyopathy and DM.

KEY FACTS

Pica intake history/ GI bleed/pregnancy, Low serum ferritin (most imp test), TIBC ↑, microcytic hypochromic, Ferritin, transferrin, Hemopexin, Hepcidin, heptoglobin, take iron with citrus juice/fruit, 2g Fe stores in females, **800mg Fe** requirement in pregnancy, Plummer wilson syndrome. Fe absorption in duodenum.

THALASSEMIA			
Alpha Thalassemia		Beta Thalassemia	
Autosomal recessive disorder, ↓ synthesis of alpha chains with relative excess of beta chains		Autosomal recessive disorder, ↓ synthesis of beta chains with relative excess of alpha chains	
Alpha globin Gene deletion on chromosome 16 is the cause		Point mutation of beta globin gene (on splice site and promotor sequence) at chromosome 11	
Alpha chains are 4, normally aa/aa. They are expressed both pre natally + post natally.		Beta chains are also 4, normally bb/bb. but expressed 6 – 9 months post – natally. Therefore anemia manifests 6 -9 months after birth	
Types of Alpha Thalassemia		Types of Beta Thalassemia	
<p>1. Silent carrier = (-/a a/a) deletion of one a-chain, asymptomatic and no anemia. Also known as alpha thalassemia minima.</p> <p>2. Alpha thalassemia trait = (-/- a/a) deletion of 2 a chain, like β-thalassemia minor. mild anemia occurs. Alpha thalassemia trait is the alpha thalassemia minor.</p> <p>3. HbH disease = (-/- -/a) characterized by precipitation of β-chain tetramers, moderate to severe Anemia occurs.</p> <p>4. Hydrops fetalis = (-/- -/-) deletion of all 4 chains, most severe of all, Incompatible with life. Characterized by precipitation of γ-chains tetramers Hb barts) Survival in early life Is due to expression of Gower-Hb. Signs of fetal distress in 3rd trimester</p> <ul style="list-style-type: none">Hydrops fetalis = gamma tetramers (γ)HbH disease = Beta – tetramers		<p>B⁰ = total absence , B+ = present but reduced synthesis.</p> <p>B-Thalassemia minor : (heterozygote, B⁰/B or B+/B-one mutated and one normal)</p> <p>Features: Mild anemia + Protective against falciparum malaria</p> <p>Diagnosis confirmed by HbA2 electrophoresis Normal HbA2 is 3 to 3.5% more than 3.5% suggests B- thalassemia minor</p> <p>B-Thalassemia major : (Cooley's anemia) Homozygous: B⁰/B⁰ or B+/B+ Severe microcytic anemia requiring blood transfusion. Excess iron/ over overload → hemochromatosis.</p> <p>Pathogenesis</p> <p>1. Extra-medullary haematopoiesis: it Leads to</p> <ul style="list-style-type: none">Marrow expansion→ crew cut appearance on skull x-ray) + Skeletal deformities/ Chipmunk" facieshepatosplenomegalyRisk of parvovirus B19-induced aplastic crisis <p>2. Ineffective Erythropoiesis: destruction of immature RBCs in circulation (hemolysis).</p> <p>Diagnosis : Hb electrophoresis: ↑ Hb F (a2, γ2) HbF is protective in the infant and disease becomes symptomatic after 6 months</p>	
Hb Electrophoresis – confirmatory test for Thalassemia			
	HbA	HbA2	HbF
Normal	97 – 99%	1 – 3%	< 1%
Thalassemia Minor/trait	80 – 95%	4 – 8%	1 – 5%
Thalassemia intermedia	0 – 30%	0 – 10%	6 – 100%
Thalassemia Major	0 – 10%	4 – 10%	90 – 96%
<p>HbA2 > 3.5% is diagnostic of thalassemia minor. In Beta Thalassemia Major: HbF is 96 – 99% and very low/ absent HbA.</p> <p>For iron overload in thalassemia: Deferoxamine, deferiprone (best)</p>			
Anemia of Chronic disease	Lead Poisoning	Sideroblastic Anemia	
Most common anemia in malignancy, alcoholism, and chronic diseases e.g RA Mech: ↑ IL – 6 → ↑ Hepcidin Peripheral blood & Iron Studies Mild: usually normocytic and normochromic Moderate: may be microcytic and normochromic	Dec. Heme synthesis and ↑ RBC protoporphyrin High risk in old houses with chipped paint, batteries and ammunition. Lead poisoning causes mental deterioration, headache, memory loss, demyelination of nerves. Symptoms of LEAD poisoning	Defect in heme synthesis within mitochondria. Iron is available but cannot incorporate it into Hb. Trapped iron forms a ring (ring Sideroblasts) Causes are: Hereditary X-linked defect in ALA gene Acquired: Chronic alcoholism, lead, vitamin B6 deficiency.	

Severe: may be microcytic and hypochromic Serum iron is low (as in iron deficiency), but the TIBC is also low Normal or inc. Serum ferritin Bone marrow Normal or increased iron stores Decreased or absent staining for iron in erythroid precursors	Lead Lines on gingivae (Burton lines) and on metaphysis of long bones on x-ray Encephalopathy and Erythrocyte basophilic stippling Abdominal colic and sideroblastic Anemia wrist drop and foot drop. Dimercaprol and EDTA -- 1st line of Treatment or antidotes/chelators.	Ringed Sideroblasts (with iron-laden, Prussian blue-stained mitochondria) seen in bone marrow ↑ Iron, normal/low TIBC, ↑ ferritin Treatment Depends on etiology X-linked: high dose pyridoxine (vitamin B6, cofactor for ALA synthase) Acquired: EPO and G-CSFs.			
Summary of Microcytic Anemia (N = Normal)					
	Serum Fe	Ferritin	Transferrin saturation	TIBC	Blood Film/Peripheral Smear
Fe def. anemia	↓	↓ ↓	↓	↑	Microcytic, Hypochromic
Thalassemia	N/↑	N/↑	N/↑	N	Microcytic, Hypochromic, basophilic stippling
Sideroblastic anemia	↑	↑	N/↑	↓	Basophilic stippling –Pb psng
Anemia of chronic disease	↓	N/↑	N	↓	Normocytic > microcytic
Iron deficiency anemia: Low iron, Low ferritin, and High TIBC---everything is Low except TIBC which is high Anemia of chronic disease: Low iron, High ferritin and Low TIBC—everything Is low except ferritin which is high Hemochromatosis: High ferritin, High iron, High percent saturation, Low TIBC- everything is high except TIBC - low					

MACROCYTIC ANEMIAS (MCV > 100 fL)		
Megaloblastic Anemia	Non – Megaloblastic Anemia	
Impaired DNA synthesis/ DNA maturation defect. Associated with Hypersegmented neutrophils	Normal DNA synthesis Not linked to Hypersegmented neutrophils	
Causes: Folate deficiency and B12 deficiency Folate deficiency is more common than B12	Causes: Chronic Alcoholism, Liver disease, Hypothyroidism (prefer Normocytic for Hypothyroidism)	
Vit. B12 (Cobalamin) Deficiency	Clinical features	Lab Findings
Stored in liver for 3 – 4 yrs. B12 binds with intrinsic factor and absorbed in terminal ileum. Vit B12 has animal source only. Causes: <ul style="list-style-type: none"> Veganism/poor dietary intake. Diphyllobothrium latum – fish tapeworm Total gastrectomy/Pernicious anemia (autoimmune) Blind loop syndrome (bacterial overgrowth in intestine) Malabsorption syndromes/ Chronic disease etc. Hypersegmented neutrophils > Peripheral neuropathy is Imp feature of Megaloblastic anemia.	Non- Neurological: Pallor, red beefy tongue, Lemon tinge of skin Optic neuritis Neurological Peripheral neuropathy. Numbness, tingling Subacute combined Degeneration of spinal cord , intact pain + temp. Ataxia, gait disturbance	↓ serum B12 ↑ Methylmalonic acid ↑ Homocysteine Raised LDH, bilirubin. Abnormal Schilling Test: Schilling test tell us about cause of B12 def. either dietary or GIT related. Impaired absorption not corrected by Intrinsic factor suggests Malabsorption excluding the dietary cause
Folate/Folic acid (B9) Deficiency	If someone is deficient in vitamin B12 and folic acid. The vitamin B12 deficiency must be treated first. Folate can lead to “steal” of B12 stores causing worsening of neuro complications (SACD). And moreover, folate can cover the haematological features of B12 def., but neurological symptoms are not reversed by folate therapy in B12 def. Anemia	
Stored in liver for 3 – 4 months only. Source: green leafy vegetables. Absorption : Jejunum Causes Malnutrition (e.g. alcoholics), Fast foods, goat milk. Malabsorption, drugs (methotrexate, trimethoprim, phenytoin)		

Inc. Requirement (hemolytic anemia, pregnancy) Lab findings: Homocysteine raised, normal Methylmalonic. No neurological symptoms.	<ul style="list-style-type: none"> Total gastrectomy causes → B12 deficiency Partial gastrectomy/gastrectomy → Fe def. Anemia. Anemia after 3 months of gastrectomy is Fe def. While after 3yrs is B12 def. Anemia.
--	--

NORMOCYTIC NORMOCHROMIC ANEMIA

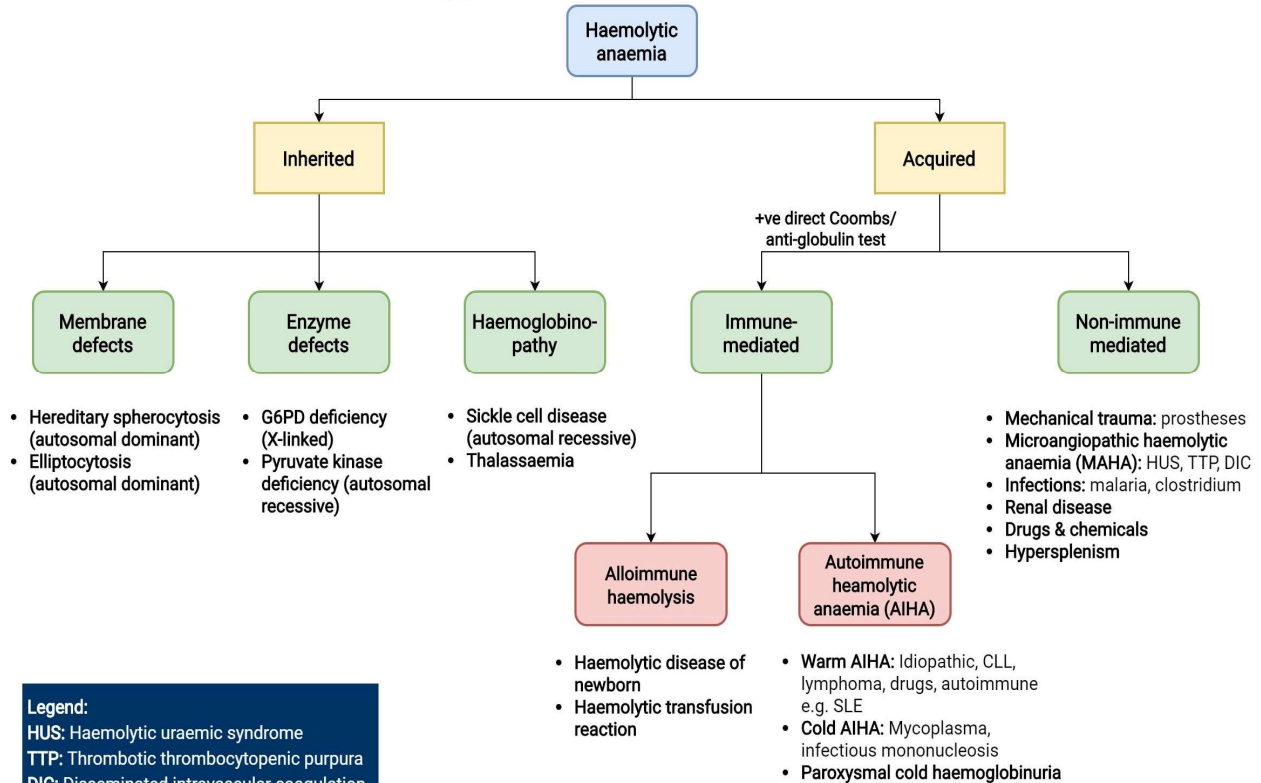
- Normocytic, normochromic anemia are classified as non hemolytic and hemolytic.
- The hemolytic anemias are further classified according to the cause of the hemolysis (intrinsic or extrinsic to the RBC) and by the location of the hemolysis (intravascular or extravascular).

APLASTIC ANEMIA

Causes	Clinical features	Labs	Treatment
<p>Caused by failure or destruction of myeloid stem cells due to:</p> <ul style="list-style-type: none"> Idiopathic Immune mediated, (1° stem cell defect). May follow acute hepatitis Radiation and drugs benzene, Chloramphenicol alkylating agents, anti metabolites Viral agents parvovirus B19, EBV, HIV, HCV Fanconi anemia (DNA repair defect), congenital 	<ul style="list-style-type: none"> Anemia = weakness + pallor Neutropenia = Infections Thrombocytopenia = Bleeding Purpura, and petechiae. <p>hepatosplenomegaly, lymphadenopathy, or bone Tenderness should not be present, and their presence should lead to review The diagnosis.</p>	<ul style="list-style-type: none"> CBC: Pancytopenia Low reticulocyte count with raised EPO Most accurate test: Trephine Bone marrow biopsy Findings: Marrow cells with fat replacement (90%) and decreased cellularity Prefer: Fatty marrow > hypocellular 	<p>Withdrawal of offending agent</p> <ul style="list-style-type: none"> Immunosuppressive regimens antithymocyte globulin (ATG) + cyclosporine (CSA) Bone marrow allograft RBC/platelet transfusion Bone marrow stimulation (GM-CSF) If age < 40 yrs. And allograft available, then do bone marrow transplant. if age more than 40, prefer ATG + Cyclosporine If no response, consider Allogenic BMT.
<p>Patients who are given Anti – Thymocyte globulin (ATG) may develop Type III HSR. (BCQ) Mechanism of action of cyclosporine = A calcineurin inhibitor → block T cell activation/inhibit T cell de-differentiation, highly nephrotoxic agent</p>			



Haemolytic Anaemia



Legend:

HUS: Haemolytic uraemic syndrome
 TTP: Thrombotic thrombocytopenic purpura
 DIC: Disseminated intravascular coagulation
 CLL: Chronic lymphocytic leukemia

GRAM PROJECT

Intravascular Hemolysis	Extravascular Hemolysis
Breakdown of RBCs in circulation/ vessels.	Breakdown of RBCs in Reticuloendothelial system (macrophages of Spleen, Liver and bone marrow)
<div>↓</div> Heptoglobin, <div>↑</div> LDH, <div>↑</div> reticulocyte, <div>↑</div> schistocytes.	<div>↑</div> LDH, <div>↑</div> Unconjugated bilirubin, <div>↑</div> Spherocytes
Hemoglobinuria/Hemosiderinuria present. Urobilinogen in urine can be present.	No Hemoglobinuria/Hemosiderinuria Urobilinogen can be found in urine
Examples mechanical hemolysis (prosthetic valves) Paroxysmal nocturnal hemoglobinuria, microangiopathic hemolytic anemia	Examples: Hereditary spherocytosis Autoimmune hemolytic anemia

IMP CONCEPTS

- ✓ **Acute hemolysis:** Dec. Heptoglobin.
- ✓ **Chronic hemolysis:** Hemosiderinuria > Hemoglobinuria.
- ✓ **Heptoglobin** binds free Hb. In intravascular hemolysis, free Hb is released into circulation. Heptoglobin binds this free Hb and this heptoglobin-Hb complex is removed by Reticuloendothelial system (mainly Spleen)
- ✓ Intravascular hemolysis yields Schistocytes and Extravascular hemolysis → Spherocytes.
- ✓ Mechanical hemolysis via prosthetic valves causes → Macroangiopathic hemolytic anemia → schistocytes on smear.
- ✓ **Microangiopathic hemolytic anemia (MAHA):** schistocytes on blood smear, seen in DIC, TTP/HUS, SLE, malignant HTN. It happens when RBCs pass through narrow lumen of vessels leading to damaged RBCs.

AUTOIMMUNE HEMOLYTIC ANEMIA (Normocytic anemia, usually idiopathic and Coomb's +ve)	
Warm Antibody Hemolytic Anemia (IgG)	Cold Antibody Hemolytic Anemia (IgM)
<p>Chronic anemia in which Primarily IgG causes extravascular Hemolysis (spherocytes on smear) Warm weather is Good. (Warm – IgG) Most commonly Warm AIHA – idiopathic 50%. May be linked to following conditions: SLE and CLL and with Certain drugs (β-lactams, alpha-methyldopa)</p> <p>Can occur in both sexes at any age but common in middle aged females Anemia of Rapid onset with fatigue, dyspnea, jaundice and splenomegaly.</p> <p>Direct Antiglobulin test/Direct Coomb's test +ve in 90% cases, most important test in warm AIHA. Spherocytes present on blood smear</p> <p>Management: Treat underlying cause 1st line – steroids 2nd line – immunosuppression via Rituximab IVIG may be used. In steroid resistant cases/recurring diseases: Splenectomy may be done.</p>	<p>acute anemia in which Primarily IgM + complement cause RBC Agglutination and extravascular hemolysis Upon exposure to cold – painful, blue Fingers and toes. Commonly idiopathic - 50% cases. but may be present in following: CLL, Mycoplasma Pneumoniae infections, infectious Mononucleosis.</p> <p>Can occur in both sexes at any age but common in middle aged females Anemia of Rapid onset with fatigue, dyspnea, jaundice and splenomegaly.</p> <p>Direct Antiglobulin test/Direct Coomb's test +ve with complement alone (C3). Blood smear shows agglutination on cold temperature. Elevated cold agglutinins titres.</p> <p>Management: Treat underlying cause, keep patient warm, avoid cold. 1st line – Rituximab (DOC) Steroids and splenectomy – ineffective.</p>
<p align="center"><u>Splenectomy</u></p> <p>Post splenectomy findings: Thrombocytosis > Howell – jolly bodies, Leucocytosis. Spherocytes persist. Hb gets Normal Overwhelming post splenectomy infections (OPSI): S. Pneumoniae > H. Influenza b > N. Meningitidis (all encapsulated) Vaccinate individuals 2 – 4weeks prior to splenectomy. In emergency cases: vaccinate 4 weeks after surgery. Life long – penicillin prophylaxis: Penicillin V 500mg 1 × b.d (use erythromycin in penicillin allergy cases.</p>	

Paroxysmal Nocturnal Hemoglobinuria	HbC disease	Pyruvate Kinase Deficiency
<p>Impaired GPI anchor synthesis leads to complement mediated lysis → hemolysis at night and Pink/red urine in the morning. Triad of: Coomb's -ve hemolytic anemia, pancytopenia, Venous thrombosis (common cause of death) High incidence of acute leukemia in PNH. Labs: CD55/C59 deficiency, RBCs on flow cytometry Ham's test is confirmatory Treat with Eculizumab (inactivates C5 to dec hemolysis)</p>	<p>Mutation in B-globin gene on chromosome 11 leads to replacement of: Glutamic acid → Lysine</p> <p>Target cells may be seen on blood smear.</p>	<p>2nd common enzyme def. Causing anemia after G6PD. Autosomal recessive. Dec ATP → rigid RBCs ↑ 2,3-BPG → ↓ O₂ affinity of Hb. Chronic and sustained hemolytic anemia in newborn Burr cell on peripheral smear.</p>

Sickle Cell Anemia	Hereditary Spherocytosis	G6PD Deficiency
<p>Point mutation affecting Beta globin gene on chromosome 11 replacing Valine with glutamic acid - at position 6 This Mutant Hb is called HbS.</p> <p>Heterozygous: HbAS -60% normal Hb, 40%HbS It is called sickle cell trait, protective against plasmodium falciparum and no anemia occurs.</p> <p>Homozygous: HbSS (HbS 100% , no normal Hb) It produces sickle cell anemia, not protective against plasmodium falciparum</p> <p>Pathogenesis: Hypoxia (low O₂), acidosis, high altitude precipitate sickling → deoxygenated HbS polymerizes) causes anemia and vaso-occlusive crisis. Intravascular + extravascular hemolysis. New-borns are initially asymptomatic due to ↑ HbF, ↓ HbS Marrow expansion due to inc. Erythropoiesis leads to Crew-cut appearance of skull on x-ray.</p> <p>Diagnosis: Hb -electrophoresis – accurate test ↑ ↑ HbS, ↑ HbF, ↓ ↓ HbA On Peripheral smear: Crescent shaped sickle cells are seen.</p> <p>Complications: Autosplenectomy (splenic sequestration) Howel jolly bodies</p> <p>Risk of Infections: Osteomyelitis by Salmonella Pneumococcal sepsis/meningitis</p> <p>Haematuria: due to sickling in renal medulla.</p> <p>Sickle cell Crisis:</p> <ol style="list-style-type: none"> 1. Aplastic crisis: due to parvo-,B19 virus, temporary arrest of erythropoiesis. 2. Painful Vaso-occlusive crisis: dactylitis, Stroke, mesenteric ischemia, priapism, Avascular necrosis, abdominal pain, backache, bone pain Acute chest syndrome – common cause of death in adults related to sickling. 3. Sequestration crisis: sudden drop in Hb levels with abdominal pain. 4. Hemolytic crisis: low Hb, jaundice and hepatosplenomegaly <p>Treatment: Hydroxy urea → inc. HbF Hydration, avoidance of triggering agents.</p>	<p>Autosomal dominant mutation of RBC membrane protein making it fragile and prone to destruction.</p> <p>Most common mutation: Ankyrin Others: Spectrin, band 3,4</p> <p>Findings & Labs: Small round RBCs with loss of central pallor → inc. MCHC Extravascular hemolysis in spleen leads to spherocytes formation. Splenomegaly, Jaundice, gallstones Coomb's test -ve Confirmatory test: +ve Osmotic fragility test → RBCs rupture when kept in hypotonic saline.</p> <p>Treatment: Splenectomy is always beneficial.</p> <p>Remember that:</p> <ul style="list-style-type: none"> • Most common mutation in HS is Ankyrin > spectrin • Main protein that maintains structural integrity of RBCs is spectrin 	<p>X-linked recessive affects males mostly, self limited disease. Most common form of enzyme deficiency anemia G6PD is rate limiting enzyme of HMP shunt → produces NADPH → keeps Glutathione in reduced form-GSH, that is protective for RBCs.</p> <p>When G6PD is deficient: Oxidative stresses (Infection, drugs and fava beans) trigger this disease. As the GSH pool is low, free radicals like H₂O₂ cause oxidation of Hb which precipitates (ppt) in the form of Heinz bodies. So, Heinz bodies = Oxidized ppt Hb.</p> <p>These Heinz bodies are removed from RBCs by splenic macrophages leading to formation of Bite cells</p> <p>Remember the sequence:</p> <ul style="list-style-type: none"> • Infections > drugs > fava beans • Drug involved are Primaquine, Dapsone, Co-trimoxazole, Sulfonamides etc. <p>Peripheral smear shows; Heinz bodies + bite cells. Confirmatory test : RBC enzyme assays or levels.</p>

COOMBS TEST (ANTIGLOBULIN TEST)

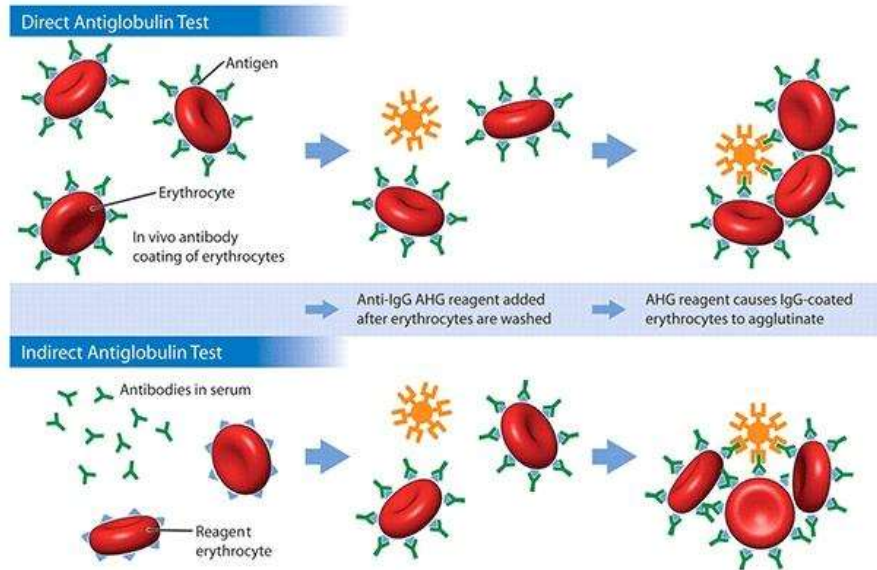
Detects the presence of antibodies against circulating RBCs.

Direct Coombs Test	Indirect Coombs Test
anti-Ig antibody (Coombs reagent) added to patient's RBCs. RBCs Agglutinate if RBCs are coated with Ig . Used for AIHA diagnosis.	Normal RBCs added to patient's serum. If serum has anti-RBC surface Ig, RBCs agglutinate when Coombs reagent is added. Used for pre transfusion testing

**Direct
Coomb's
Test**

VS

**Indirect
Coomb's
Test**



HEMOLYTIC DISEASE OF THE FETUS AND NEWBORN (Erythroblastosis fetalis)

Rh hemolytic disease	ABO hemolytic disease
<ol style="list-style-type: none"> 1. Mother: Rh -ve, Fetus: Rh +ve 2. First pregnancy: mother exposed to fetus +ve blood, mostly during delivery, leads to formation of maternal anti-D IgG In subsequent pregnancies: anti-D IgG crosses placenta, attacks fetal and newborn RBCs leading to hemolysis. 3. Presentations: Hydrops fetalis, jaundice shortly after birth and kernicterus. 4. Prevent by administering anti-D IgG to Rh -ve pregnant mothers during 3rd trimester + early post-partum period if fetus is Rh +ve. It prevents maternal anti-D IgG production. 	<ol style="list-style-type: none"> 1. Mother: O blood group, Fetus: type A or type B 2. Pre-existing anti-A and/or anti-B IgG antibodies in pregnant patient cross the placenta to attack fetal and newborn RBCs causing hemolysis. 3. Presents with jaundice within 24 hrs of birth Unlike Rh hemolytic disease, it may occur in first born babies as well and usually less severe. 4. Treated with phototherapy or exchange transfusion with -ve blood group. For example for newborn with A+ blood group, exchange transfusion will be done with A -ve group.

QUICK RECAP OF RBCs disorders

- ✚ MCV less than 80 fL in microcytic anemias → Thalassemia, Fe def., anemia of chronic disease, sideroblastic.
- ✚ MCV normal 80-100 fL in normocytic anemia : aplastic, autoimmune, G6PD, Sickle cell, HS, PNH, PK def.
- ✚ MCV > 100 fL in macrocytic anemias → may be Megaloblastic (B12/Folate def.) Or Non-Megaloblastic (Liver disease, alcoholism, hypothyroidism).
- ✚ Hypersegmented neutrophils are the specific feature of megaloblastic anemia.
- ✚ Anemia in acute blood loss or hemorrhage is = Normocytic-normochromic anemia.
- ✚ Anemia of chronic disease is mostly normocytic (if severe, then microcytic). IL – 6 causes inc. Hepcidin.
- ✚ ↑ Methylmalonic acid ↑ Homocysteine ↓ serum B12 + neurological symptoms → Vit B12 def.
- ✚ ↑ Homocysteine, normal MMA, no neurological features in → Folate deficiency.
- ✚ Anemia in hypothyroidism is mostly normocytic-normochromic type.
- ✚ Target cells seen in thalassemia and pencil cells in iron def. Anemia
- ✚ Triad of Fe def. Anemia + dysphagia + Esophageal webs → Plummer wilson syndrome.
- ✚ Burr cells are seen in CKD and pyruvate kinase deficiency. Bite cells in G6PD def.
- ✚ Hb synthesis starts in Pro-erythroblast > early normoblast. Hb appears in intermediate normoblast. Hb synthesis is max in late normoblast whereas max Hb conc. In reticulocytes.
- ✚ Normal shape of RBCs is biconcave, avg diameter 7.5 um.
- ✚ Life span of ~120 days in healthy Adults; 60-90 days in neonates.
- ✚ Howel – jolly bodies are feature of Splenectomized individuals e.g sickle cell anemia
- ✚ Inc. MCHC, loss of central pallor and spherocytes are feature of Hereditary spherocytosis.
- ✚ Most common mutation in HS is Ankyrin gene mutation, whereas Spectrin is most important for membrane stability/integrity of RBCs. Band 3 is involved in HCO₃/Cl exchange process.
- ✚ Fatty marrow 90% > hypocellular marrow is mandatory for diagnosis of aplastic anemia.
- ✚ Warm AIHA is via IgG and Cold AIHA by IgM. Cold agglutinins raised in cold AIHA (e.g mycoplasma infection)
- ✚ Schistocytes seen in both micro + macro angiopathic hemolytic anemias.
- ✚ Prosthetic heart valves lead to macroangiopathic hemolytic anemia.
- ✚ Salmonella osteomyelitis may happen in Sickle cell disease.
- ✚ Cause of sickle cell anemia is point mutation in the B globin gene at chromosome 11
- ✚ Sickle cell anemia + thalassemia may coexist together in a patient, called sick-thalassemia syndrome. Because both are due to defect of Beta globin chains.
- ✚ Specific feature of G6PD def. Is acute self limited hemolysis. Infection > drugs are prominent causes.
- ✚ Decrease heptoglobin is seen in acute intravascular hemolysis e.g G6PD def.
- ✚ Feature of acute hemolysis → Dec. Heptoglobin, in chronic hemolysis → hemosiderinuria > hemoglobinuria.
- ✚ Anemia in CKD is anemia of chronic disease → Normocytic-normochromic with dec. EPO, give S/C EPO.
- ✚ People solely depending on fast foods may develop folic acid def. Also goat milk has low folate.
- ✚ Low MCV, low MCH, low MCHC is seen in iron def. Anemia. (Raised TIBC + platelets)
- ✚ Basophilic stippling is seen in sideroblastic (Pb poisoning) anemia.
- ✚ HbA₂ > 3.5% is seen in thalassemia minor.
- ✚ Hb electrophoresis is confirmatory test for thalassemia and sickle cell disease.
- ✚ Specific secondary granules are seen in Myelocyte stage.
- ✚ Hematopoietic stem cells (HSCs) are differentiated on the basis of CD34.
- ✚ HSCs on myelocytic stage are differentiated on basis of staining of granules.
- ✚ Direct antiglobulin test/Coomb's test is +ve in hemolytic anemia.
- ✚ For aplastic anemia, If age > 40, give anti-thymocyte globulin + cyclosporine.
- ✚ Strict vegetarian diet puts at risk of B12 def.
- ✚ Methotrexate, trimethoprim, phenytoin may lead to folate def.
- ✚ Dapsone + Primaquine may cause G6PD def. Anemia.
- ✚ Hereditary cause of sideroblastic anemia is ALA – synthase deficiency.
- ✚ Osmotic fragility test +ve in Hereditary spherocytosis.
- ✚ Beta chains tetramers seen in HbH disease
- ✚ Gamma chain tetramers in Hydrops fetalis --- incompatible with life.
- ✚ Anti tumor and anti viral cells part of innate immunity are NK cells.

- ✚ Cells providing immunity against Covid-19 are NK cells.
- ✚ Basophilia is a feature of CML.
- ✚ Allergy + asthma + parasites cause eosinophilia.
- ✚ Lymphocytes are raised in viral infections.
- ✚ Total gastrectomy may cause B12 def. and partial gastrectomy leads to iron def. Anemia.
- ✚ Reticulocyte index depicts the bone marrow activity/efficiency.
- ✚ Reticulocyte index informs about bone marrow erythropoietic activity.
- ✚ Antibody involved in hemolytic disease of new-born is IgG.
- ✚ In excessive hemolysis, raised bilirubin may cause kernicterus → basal ganglia staining.
- ✚ RHOGAM-D injection is given in 3rd trimester.
- ✚ If mother is Rh +ve and child Rh-ve, there is no risk of haemolytic disease of newborn (HDN)
- ✚ HDN manifest at 2nd pregnancy.
- ✚ Hemolytic reaction/incompatibility manifesting at 1st pregnancy is → ABO incompatibility.
- ✚ LAP score is raised in acute leukemoid reactions (infections) and dec. LAP score in CML.
- ✚ Iron homeostasis is via ferritin, controlled by Hepcidin and maintained by transferrin.
- ✚ Normal storage form of iron is ferritin (soluble).
- ✚ Normal Fe requirement in pregnancy: 800mg and for calcium 1200mg
- ✚ Most common cause of low Hb in pregnancy is → Normal physiological anemia of pregnancy > Fe deficiency.
- ✚ Normal body iron stores are 4g, 6g in males and 2g in females
- ✚ Embryonic Hb has 2 zeta + 2 epsilon chains. Fetal Hb has 2 alpha + 2 gamma chains.
- ✚ Take iron preferably with Citrus fruit/juice > empty stomach. Meat is a rich source of iron.
- ✚ Drugs are taken with meal to reduce gastric upset.
- ✚ Porphyria cutanea tarda is due to UPG decarboxylase def. Leading to accumulation of Uroporphyrin.
- ✚ In HDN, Test to be done on Baby is direct coombs and indirect in mother serum to check presence of antibodies.

DISORDERS OF WBCS

Leukemia	Lymphoma	Leukemoid Reaction
Lymphoid or myeloid neoplasm with widespread bone marrow involvement. Tumors cells are usually found in peripheral blood.	Discrete tumor mass arising from lymph nodes with variable presentation (arising in atypical sites, leukemic features sometimes are also there).	Acute inflammatory response to infections leading to raised TLC, <div style="background-color: #007bff; color: white; padding: 2px 5px; display: inline-block;">↑</div> Band cells (left shift) and high LAP score.

LYMPHOMAS

(Classified into Hodgkin and Non-Hodgkin lymphoma)

Lymph node biopsy is the gold standard for diagnosis.

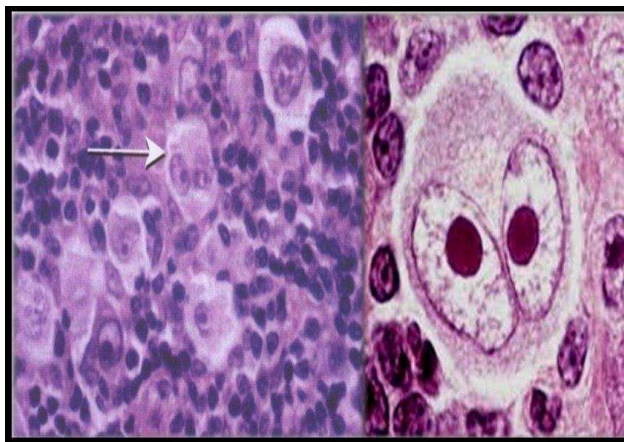
HODGKIN LYMPHOMA (HL)				NON-HODGKIN LYMPHOMA (NHL)	
<div>1. Characterized by Reed – Sternberg cells (tumor giant cells)</div> <div>2. Painless localized, single group of LNs involvement. Lymph nodes are rubbery in nature Cervical/supraclavicular 60-80%, axillary, inguinal.</div> <div>3. Contagious spread, Better prognosis Staging is stronger predictor of prognosis.</div> <div>4. Associated with EBV (common in Africa)</div> <div>5. Bimodal age distribution: young adulthood and >55 yr More Common in males except for nodular sclerosis type that is more common in females</div> <div>6. Pel-Ebstein fever: high grade fever for 1-2 wk followed by afebrile period of 1-2 wk.</div>				<div>1. No Reed-Sternberg cells. Majority involves B cells and a few are T cell NHL. (B cell NHL 80%, T cell NHL 20%)</div> <div>2. Multiple LNs involved + extra nodal involvement is common.</div> <div>3. Non-contagious spread + worse prognosis.</div> <div>4. Associated with autoimmune diseases (SLE, RA) and viral infections (HIV, HTLV, EBV).</div> <div>5. Can occur in children and adults at any age, mostly in 20-40 years of age.</div> <div>6. Patients with Burkitt lymphoma have jaw swelling, abdominal pain/fullness. Testes/CNS involvement may be present.</div>	
Classification of HL (5 types)				Classification of NHL (On the basis of cell type)	
<u>Classical HL</u>		<u>Non-Classical HL</u>		<u>Neoplasm of Mature B cells</u>	<u>Neoplasm of Mature T cells</u>
<div>1. Nodular sclerosis</div> <div>2. Mixed cellularity</div> <div>3. Lymphocytic rich</div> <div>4. Lymphocytic depleted</div>		<div>• Lymphocytic predominant – best prognosis , pop corn cell present.</div>		<div>1. Burkitt lymphoma</div> <div>2. Diffuse large B cells lymphoma</div> <div>3. Follicular lymphoma</div> <div>4. Mantle cell lymphoma</div> <div>5. Marginal lymphoma</div>	<div>1. Adult T cell lymphoma</div> <div>2. Mycosis fungoides or sezary syndrome</div>
Staging (Ann-Arbor)					
Stage I	Stage II	Stage III	Stage IV		
Single lymph node involvement.	2 or more LNs involved on same side of diaphragm	More than 2 LNs involved on both side of diaphragm. With Spleen	Extra nodal involvement or distant metastasis E.g Liver		

Staging	
An-Arbor staging, same as HL.	
Overall NHL are common than HL and constitutional (B) symptoms like fever, weight loss and night sweats are more pronounced in HL than NHL.	

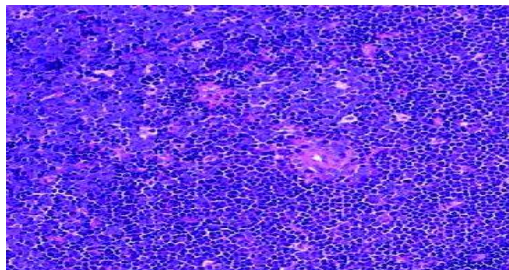
Reed Sternberg Cells:

A special feature of Hodgkin lymphoma, they are Bilobed/binucleated tumor giant cells with 2 halves behaving as mirror image giving the **appearance of Owl's eye**.

Remember that Owl's eye **inclusions** are seen in CMV infection.



Type of Hodgkin lymphoma	Features
1. Nodular sclerosis	Most common type, more common in females, EBV -ve , excellent prognosis. Cervical/supraclavicular LNs more involved, Reed-Sternberg cells + fibrotic bands present making lacunar pattern.
2. Mixed cellularity	2 nd common type, more incidence in males, strong link with EBV 70%. Better prognosis. Reed-Sternberg cells seen, eosinophils present, no lacuna present
3. Lymphocytic rich	More common in old males, EBV +ve 30%, Good prognosis, RSC present with abundant lymphocytes.
4. Lymphocytic depleted	Worst prognosis, EBV +ve , Reed-Sternberg cells + diffuse fibrosis.
5. Lymphocytic predominant	More incidence in young males, Best prognosis, EBV -ve , Pop corn cells/LP are present (not typical Reed-Sternberg cells). CD45+
Type 1 – 4 HL are CD15+ & CD30+ whereas Lymphocytic predominance type has CD45+	
Types of Non-Hodgkin Lymphoma (NHL)	
Neoplasm of Mature B cells	<ol style="list-style-type: none"> Burkitt Lymphoma: C-Myc translocation, t (8;14). C-Myc (8) – Heavy chain (14) EBV association, Starry-sky appearance, sheet of lymphocytes with tangible body macrophages as shown in figure below. Endemic form: painless jaw lesion – in Africa Sporadic form: Abdominal/Pelvic masses Diffuse Large B cell lymphoma: most common type in adults, mutation in BCL -2 and BCL-6 Follicular Lymphoma: t (14;18) – translocation of heavy chain Ig (14) and BCL-2 (18) Painless waxing + waning lymphadenopathy. Marginal lymphoma: t (11;18), associated with chronic inflammation e.g MALT lymphoma in H.pylori is marginal lymphoma. Mantle cell lymphoma: t (11;14), translocation of cyclin D1 with heavy chain (14) , CD5+ Very aggressive – patient presents at late stage of disease. Primary CNS lymphoma: An AIDS defining illness, EBV related in HIV/AIDS. Single ring enhancement lesion on MRI brain
Neoplasm of Mature T cells	<ol style="list-style-type: none"> Adult T cell lymphoma: Cause = Human T cell leukemia virus (HTLV) Common in Japan, Africa and Caribbean, typically present with skin lesions, lytic bone lesion and hypercalcemia Mycosis fungoides/sézary syndrome: Skin patches + plaques (cutaneous T cell lymphoma) Atypical CD4+ present with Cerebriform nuclei. Intra epidermal neoplastic cell aggregates → Pautrier micro abscesses May progress to sezary syndrome (T cell leukemia)



LEUKEMIAS

- Unregulated growth and differentiation of WBCs in bone marrow/peripheral blood → marrow failure.
- Consequently, Anemia (low RBCs), infections (low mature WBCs), bleeding (low PLT) occur.
- WBCs are usually high in count (± 1 lac), but they are malignant and immature (blast cells) with infiltrations in liver, spleen, lymph nodes, skin and other organs commonly.
- Some cases present with normal or low WBCs count.
- Bone marrow examination and immunophenotyping is vital to diagnose leukemias.

Acute Leukemia		Chronic Leukemia	
Failure of cell maturation leads to: Blast cells > 20% in bone marrow Examples: AML & ALL.		Insidious onset of marrow failure leads to: < 20% blast cells in marrow. Examples: CML & CLL.	
Acute Lymphoblastic leukemia (ALL)	Acute myeloid leukemia (AML)	Chronic Lymphocytic leukemia (CLL)	Chronic myeloid leukemia (CML)
<ul style="list-style-type: none"> • Age: 1-14 years mostly. Most common malignancy in children overall is ALL • ↑ lymphoblasts (B/T cell) • Have Granular cytoplasm • B cells ALL > T cells ALL • CD10+: marker of pre-B cells • TdT + and CALLA +ve • Association of ALL with Down syndrome. • Clinical features: Bone pain, tenderness, Infections (fever), pallor, bleeding (epistaxis), hepato-splenomegaly, Lymphadenopathy T-ALL may present with mediastinal mass or spread to CNS/Testes. • ALL is most responsive to treatment i.e good prognosis. • t(12;21): good prognosis • t(9;22) → poor prognosis • younger age and WBCs less than 50K in B-ALL and less than 100K in T-ALL are good prognosis factors. • FAB classification categorizes ALL into L1, L2, L3. 	<ul style="list-style-type: none"> • Age: 15-40 (rarely 50+) • Prior radiations and Chemotherapy are risk factors. • Auer rods (Azurophilic) granules present • ↑ myeloblasts in bone in peripheral smear • Granular cytoplasm and MPO +ve stain • Sudan black B +ve • FAB classification divides AML into M0-M8 • M3 is acute Promyelocytic leukemia (APL), presents with DIC mostly • All trans retinoic acid (Vit A) and arsenic trioxide are helpful in M3 treatment • Association with Down's syndrome: M7 • Translocation 15;17 is seen in M3 / APL, has good prognosis. • Poor response to chemotherapy. 	<ul style="list-style-type: none"> • Age: 50-60 years. • Most common adult leukemia • B cell neoplasm, CD10-ve • CD20+, CD23+, CD5+ • Most common cause of generalized lymphadenopathy • Associated with radiations + auto immune hemolytic anemia. • CLL may transform into aggressive diffuse large B cell lymphoma, known as Richter's syndrome. • CBC: <ul style="list-style-type: none"> • Inc lymphocytosis $> 5 \times 10^9/L$ • Blast cells <5% • Peripheral smear: <ul style="list-style-type: none"> • Smudge cells or parachute cells, they are crushed little lymphocytes (lab artefact) • CLL is also known as small lymphocytic leukemia (SLL), but the difference is that CLL has Inc peripheral Lymphocytes + bone marrow involvement. 	<ul style="list-style-type: none"> • Age: 65+ mostly • Patient complaints of fever, night sweats and fatigue – no infection. • ABL – BCR Is required for diagnosis • Philadelphia chromosome: t(9;22), involves fusion of ABL proto-oncogene on chromosome 9 with Break cluster region of chromosome 22 • If Philadelphia chromosome is absent → poor prognosis. • Responds well to BCR-ABL tyrosine kinase inhibitors (imatinib) • CBC: raised TLC especially: <ul style="list-style-type: none"> • Basophilia + eosinophilia • Presents with: dysregulated production of mature + maturing lymphocytes i.e • Neutrophils, myelocytes and metamyelocytes all are raised. • LAP score: <ul style="list-style-type: none"> • Decreased • Massive Splenomegaly is present. • May accelerate and transform into AML > ALL -- Known as blast crisis – most common cause of death. • Transformation in AML carries poor prognosis

Hairy Cell leukemia

- Mature B cell tumor in elderly patients, tumor cells have filamentous hair like projections.
- Patient presents with massive splenomegaly + marrow fibrosis – dry tap on aspiration + pancytopenia.
- Stains **TRAP +ve** (tartrate – resistant acid phosphatase). Also linked with BRAF mutations.
- Treated with purine analogues (cladribine + pantostatin)

Quick Recap + Imp Concepts --- Leukemia & Lymphoma

- ✓ Lymphoid neoplasms involve lymphocytes proliferation e.g ALL, CLL and hairy cell leukemia.
- ✓ B cell neoplasm are more common than T cell e.g B-ALL is more common than T-ALL.
- ✓ Myelogenous/myeloid neoplasms involve cell lines derived from common myeloid origin → Granulocytes (neutrophils, basophils, eosinophils) + erythroblasts (RBCs precursors) + megakaryoblasts (platelets precursor)
- ✓ Blast cells may be lymphoblasts or myeloblasts depending upon type of disorder.
- ✓ > 20 % blast cells are mandatory for establishing diagnosis of acute leukemia
- ✓ Leukemia commonly associates with radiations is CLL – also most common adult leukemia is CLL.
- ✓ Leukemia is the most common malignancy in children followed by gliomas (2nd) and Ewing's sarcoma (3rd)
- ✓ Most common leukemia in children is ALL. B cell ALL being more common than T cell ALL
- ✓ Generally, age 1-14 → ALL, 15-40 → AML (sometimes 50+), age 65+ → CML, age 50-60 → CLL.
- ✓ T cell leukemias present with mediastinal mass or infiltration of CNS/ Testes etc.
- ✓ Lymphocytes are agranulocytes, so their cytoplasm lacks granules. So lymphoblasts cytoplasm lacks granules whereas myeloblasts contain cytoplasmic granules.
- ✓ Basophilia (raised basophils) is a feature specifically seen in CML. Eosinophilia, Metamyelocytes also present.
- ✓ Massive splenomegaly is seen in CML (M in CML for Massive).
- ✓ Special stains are used to see characteristics features e.g Auer rods in AML by Sudan black.
- ✓ ALL is Tdt +ve and CALLA +ve. Commonly presents with infection, bleeding, pallor in children age 2-14.
- ✓ Smudge cell/ parachute cells are a special feature of CLL..ALL involves Blasts cells, CLL involves mature lymphocytes
- ✓ Generalized fatigue in adults/ elderly is common in CLL
- ✓ CML is a myeloproliferative disorder and also classified with it.
- ✓ AML and ALL are associated with Down's syndrome (AML > ALL)
- ✓ Marker of pre-B cells in ALL: CD10+
- ✓ Marker of mature B cells: CD19+, CD20+.
- ✓ AML; M3 presents with DIC. Gum bleeding is mainly seen in AML; M5.
- ✓ BCR-ABL fusion > Philadelphia t (9;22) is required for diagnosis of CML
- ✓ CML responds well to tyrosine kinase inhibitors i.e Imatinib.
- ✓ Hairy cell leukemia is a mature B cell neoplasm, dry tap on aspiration + massive splenomegaly.
- ✓ ALL is most responsive to therapy or having better prognosis than all others.
- ✓ Overall Non-Hodgkin lymphoma are more common than HL
- ✓ Reed-Sternberg cells (binucleated, bilobed, owl eye's appearance) are specific features of Hodgkin lymphoma.
- ✓ Nodular sclerosis is most common HL, common in females and involves cervical/supraclavicular lymph nodes.
- ✓ Pop-corn cells are seen in lymphocyte predominant HL, CD45+.
- ✓ Hodgkin Lymphoma with best prognosis is lymphocyte predominant.
- ✓ Ann-Arbor staging is done for lymphoma, Spleen involved in stage III mainly.
- ✓ Diffuse large B cell lymphoma (DLBCL) is most common type of NHL.
- ✓ T (14;18) in follicular lymphoma, t (11;14) in mantle cell lymphoma and t (11;18) present in marginal cell lymphoma.
- ✓ Mixed cellularity lymphoma is strongly linked to EBV (in HIV/AIDS).
- ✓ Pautrier micro abscesses, CD4+ cells with cerebriform nuclei are features of mycosis fungoides (mature T cell tumor).
- ✓ Most common type of leukemia in adults in CLL whereas MC type of acute leukemia in adults is AML
- ✓ French-American-British (FAB) classification system categories AML into M1 to M7 and ALL into L1, L2, L3.
- ✓ Mutation in BCL – 2 → Diffuse large B cell lymphoma, Over-expression of BCL -2 → Follicular lymphoma.

Classification of AML:

- M0 = undifferentiated AML (5%)
- M1 = greater no. Of myeloblasts with < 10% myelocytic differentiation.
- M2 = myeloblasts with > 10% myelocytic differentiation, neuron specific enolase < 20 % .
- AML; M3 = Acute Promyelocytic leukemia - APL (t - 15;17) – DIC common presentation.
Treated with As trioxide + all trans- retinoic acid.
- Abundant Auer rods in AML; M3,
- AML; M4 = less Auer rods, > 20% butyrate positivity in monocytic cells.
- AML; M5 = acute monocytic leukemia (gum bleeding), AML
- AML; M6 = acute erythroblastic leukemia
- AML; M7 = acute megakaryocytic leukemia – association with down's syndrome.
- AML is associated with chemotherapy.

Myelodysplastic Syndrome (MDS)

Stem cell disorder involving ineffective haematopoiesis.
Defect in cell maturation of non-lymphoid lineages.
 Pancytopenia with abnormal shaped of RBCs (macro-ovalocytes/Sideroblasts), WBCs (bilobed neutrophils) and giant platelets.
 This Bilobed appearance of neutrophils is called pseudo-Pegler huet anomaly.
Bone marrow blast cells < 20 %.
Risk of transformation into AML (blast cells > 20 %)
 Bone marrow is dysplastic, normocellular/hypercellular.
 Hypocellular bone marrow + pancytopenia= aplastic Anemia
Hypercellular marrow + pancytopenia = myelodysplasia.
 Risk factors include: chemotherapy, benzene, radiations.

Myeloproliferative Disorders (MPDs)

Hematopoietic stem cells mature normally, but excessive Clonal expansion occurs in association with JAK – 2 mutation commonly, except CML (BCR-ABL fusion).

Classification:

1. **RBCs** → Polycythemia Rubra Vera
2. **WBCs** → CML (discussed earlier)
3. **Platelets** → Essential thrombocythemia
4. **Fibroblasts** → Myelofibrosis.

Polycythemia Rubra Vera (PRV)

- Primary Polycythaemia with low EPO levels
- Acquired JAK – 2 Mutation → Raised Red cells mass and hematocrit.
- WBCs + PLT count may or may not increase.
- **WHO criteria of diagnosis = Major criteria + 1 of minor criteria.**
- **Major criteria** = Presence of JAK-2 mutation + Hb > 18.5 in M and > 16.5 in FM.
- **Minor criteria** = low EPO levels, Hypercellular bone marrow with inc. Tri lineage (RBCs, WBCs, PLT), endogenous Erythroid colony formation in vitro.
- **Clinical Features:** Plethora (Red) of face, Pruritus after hot bath , blurred vision, ringing in ears. Rare but classic symptoms is erythromelalgia (severe burning pain + red-blue discoloration due to episodic clot formation in vessels of limbs).
- Thrombotic complications like MI, Stroke, pulmonary embolism & DVT may occur due to thrombocytosis and hyper viscosity of blood.
- Gout due to raised cell turnover.
- Inc histamine leads to pruritus and peptic ulcer disease even in PRV.
- **1** Erythropoietin levels (EPO), Raised LAP score. Spleenomegaly.
- Transition to myelofibrosis > acute leukemia may occur.
- **Treatment:** phlebotomy to keep Hematocrit less than 45%, hydroxyurea, allopurinol, JAK-1/2 inhibitors (e.g. ruxolitinib).

Essential Thrombocythemia

- Increased in platelets with or without increase in WBC and RBC
- Characterized by clonal proliferation of megakaryocytes leading to persistently elevated platelets with abnormal function.
- May present with Thrombosis, hemorrhage, microvascular occlusion, erythromelalgia.
- Bone marrow: megakaryocytic hyperplasia
- **Primary thrombocytosis refers to essential thrombocythemia.**
- Secondary thrombocytosis also known as reactive thrombocytosis.
- Cause of secondary thrombocytosis are Inflammation (RA, IBD), Infection and Post splenectomy.

Primary Myelofibrosis

- Atypical megakaryocytic hyperplasia → ↑ TGF-Beta secretion → inc. Fibroblastic activity → Excessive bone marrow fibrosis leading to marrow failure.
- Massive splenomegaly + Tear drops cells are characteristics. JAK-2 mutation 50% cases.
- Dry tap on bone marrow aspiration. Marrow aspiration shows severe fibrosis replaced by reticulin and collagen.
- Dry tap is seen in myelofibrosis, Hairy cell leukemia, aplastic anemia and metastasis

Summary of Myeloproliferative disorders

	RBCs/Hct	RBC morphology	WBCs	Platelets	Philadelphia Chromosome	JAK – 2 Mutation	Bone Marrow
Polycythemia Vera	↑	N	↑	↑	-	+	Hypercellular
CML	↑/N	N	↑	↑	+	-	Hypercellular
Essential thrombocythemia	N	N	N/↑	↑	-	+	Megakaryocyte Hyperplasia
Primary Myelofibrosis	↓	Abnormal	Variable	Variable	-	+	Dry tap

Myelophthisis

It refers to the displacement of hematopoietic bone-marrow tissue into the peripheral blood, either by fibrosis (myelofibrosis), tumors, or granulomas. A myelophthisic blood smear is one which contains nucleated red blood cells, granulocyte precursors, and teardrop-shaped erythrocytes.

POLYCYTHEMIA

Type	Features						
Primary Polycythemia (P. Rubra Vera)	JAK-2 mutation, plethora/pruritus/visual disturbance, erythromelalgia, splenomegaly ↑↑ RBC mass, ↑ plasma volume, ↓ EPO, O ₂ sat unaffected. Raised other cell lines. Low EPO due to -ve feedback suppressing renal EPO production						
Secondary Polycythemia	<p>No JAK-2 mutation, no splenomegaly, normal other cell lines, associated with high altitude, Lung/heart disease, EPO secreting tumors rarely, Carboxy-Hb. Two types as follows;</p> <table> <tr> <th>Appropriate Absolute type</th><th>Inappropriate Absolute type</th></tr> <tr> <td>Seen in high altitude, Lung/congenital heart diseases.</td><td>Exogenous EPO: athletes (blood doping) EPO secreting tumors, RCC/ HCC etc.</td></tr> <tr> <td>↑ RBC mass, ↑ EPO, ↓ O₂ saturation Plasma volume is unaffected.</td><td>↑ RBC mass, ↑ EPO, O₂ sat and plasma volume are normal.</td></tr> </table>	Appropriate Absolute type	Inappropriate Absolute type	Seen in high altitude, Lung/congenital heart diseases.	Exogenous EPO: athletes (blood doping) EPO secreting tumors, RCC/ HCC etc.	↑ RBC mass, ↑ EPO, ↓ O ₂ saturation Plasma volume is unaffected.	↑ RBC mass, ↑ EPO, O ₂ sat and plasma volume are normal.
Appropriate Absolute type	Inappropriate Absolute type						
Seen in high altitude, Lung/congenital heart diseases.	Exogenous EPO: athletes (blood doping) EPO secreting tumors, RCC/ HCC etc.						
↑ RBC mass, ↑ EPO, ↓ O ₂ saturation Plasma volume is unaffected.	↑ RBC mass, ↑ EPO, O ₂ sat and plasma volume are normal.						
Relative Polycythemia	Association with dehydration, burns/stress → fluid loss. RBC mass is unaffected/normal. ↓ ↓ plasma volume, normal RBCs, normal O ₂ saturation and normal EPO levels.						

PLASMA CELL DYSCRASIAS

- As plasma cell produce antibodies/immunoglobulins. So, these disorders are characterized by overproduction of monoclonal immunoglobulins/para-proteins (also called Para-proteinemias)
- Gammopathy = overproduction of one or more class of Immunoglobulins.
- **Monoclonal Gammopathy** = a single clone of plasma cell produces **identical** Immunoglobins (Ig).
- Monoclonal Immunoglobins are called M-proteins/Para proteins.
- **Polyclonal Gammopathy** = a single clone of plasma cells produces **different** Ig.
- Labs: serum protein electrophoresis (SPEP) Or free light chain (FLC assay for initial tests
- (M Spike on SPEP represents overproduction of a monoclonal Ig fragment).
- For urinalysis, use 24-hr Urine Protein electrophoresis (UPEP) to detect light chain.
- **Confirm with bone marrow biopsy.**

Multiple Myeloma (MM)	<p>Overproduction of IgG and IgA (IgG 60% of cases > IgA). Presents with backache (punched out lytic lesion on X-ray spine), Hypercalcemia, anemia, Renal involvement. CRAB = Hypercalcemia, Renal injury, Anemia, bone lytic lesion. Peripheral smear: Shows Rouleaux formation – RBCs stacked/piled up. Urine analysis: Bence Jones proteins in urine → Ig light chains. -ve urine dipstick stick test (because it detects albumin only). Bone marrow analysis shows: >10% monoclonal plasma cells having clock-face chromatin + intracytoplasmic inclusions containing IgG. Protein Electrophoresis shows : large, IgG - M spike formation. Complications include: risk of infection + primary amyloidosis (AL type) Beta-2 microglobulin and LDH levels reflect tumor burden.</p>
Waldenstrom Macroglobulinemia (WM)	<p>Also known as lymphoplasmacytic lymphoma → B cells neoplasms secreting monoclonal IgM and therefore IgM – M spike is seen. Bone marrow shows >10% small lymphocytes with intranuclear pseudo inclusions containing IgM. Clinical features: No bone lesions/hypercalcemia (No CRAB findings). Hyperviscosity syndrome: 80 % cases of Hyperviscosity syndrome are due to WM. Its features are: Headache, blurred vision, retinal hemorrhages, Raynaud's phenomena. Thrombosis is a feared complication.</p>
Monoclonal gammopathy of undetermined significance (MGUS)	<p>Most common monoclonal gammopathy, overproduction of any Ig type, usually asymptomatic, NO CRAB findings, no urinary bence jones proteins. < 10 % monoclonal plasma cells on bone marrow analysis 1% Risk per year of conversion into MM.</p>

CRYOGLOBULINAEMIA

- Immunoglobulins which undergo reversible precipitation at 4 C, dissolve when warmed to 37 C.
- One-third of cases are idiopathic.

Type 1 (25%)	Type 2 (25%)	Type 3 (50%)
Monoclonal IgG/IgM	Mixed monoclonal and polyclonal: usually with rheumatoid factor (RF)	Polyclonal: usually with RF
Associations: multiple myeloma, Waldenstrom macroglobulinaemia	Associations: Hepatitis C, RA, Sjogren's, lymphoma	Associations: rheumatoid arthritis, Sjogren's
Symptoms	Labs	Treatment
Symptoms (if present in high concentrations) Raynaud's only seen in type 1 Cutaneous: vascular Purpura, distal ulceration, ulceration Arthralgia Renal involvement (diffuse glomerulonephritis)	Low complement (especially C4) High ESR.	Immunosuppression Plasmapheresis

IGG4 Related Diseases

- IgG4-related disease has been described in virtually every organ system: the biliary tree, salivary Glands, periorbital tissues, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, Pericardium, and skin.
- The histopathological features are similar across organs, regardless of the Site.
- IgG4-related disease is analogous to sarcoidosis, in which diverse organ manifestations are Linked by similar histopathological characteristics.
- Raised concentrations of IgG4 in tissue and serum Can be helpful in diagnosing IgG4 disease, but neither is a specific diagnostic marker

Examples:

- Riedel's Thyroiditis
- Autoimmune pancreatitis
- Mediastinal and Retroperitoneal Fibrosis
- Periaortitis/periarteritis/inflammatory aortic aneurysm
- Kuttner's Tumour (submandibular glands) & Mikulicz Syndrome (salivary and lacrimal glands)
- Possibly Sjogren's and primary biliary cirrhosis

TUMOUR LYSIS SYNDROME

- (TLS) is a potentially deadly condition related to the treatment of high-grade Lymphomas and leukemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion, it can occur with steroid treatment Alone.
- TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from The cell, It leads to a high potassium and high phosphate level in the presence of a low calcium. It Should be suspected in any patient presenting with an acute kidney injury in the presence of a high Phosphate and high uric acid level.
- Patients at high risk of TLS should be given IV allopurinol or IV rasburicase immediately prior to and During the first days of chemotherapy (should not be given together in the management of tumour lysis syndrome as this Reduces the effect of rasburicase).Treatment relies on Allopurinol or rasburicase and hydration.
- From 2004 TLS has been graded using the Cairo-Bishop scoring system

Laboratory TLS	Clinical TLS
<p>abnormality in two or more of the following, occurring within</p> <p>Three days before or seven days after chemotherapy.</p> <p>Uric acid > 475umol/l or 25% increase</p> <p>Potassium > 6 mmol/l or 25% increase</p> <p>Phosphate > 1.125mmo/l or 25% increase</p> <p>Calcium < 1.75mmol/l or 25% decrease</p>	<p>laboratory tumour lysis syndrome plus one or more of the following:</p> <ul style="list-style-type: none"> • Increased serum creatinine (1.5 times upper limit of normal) • Cardiac arrhythmia or sudden death Seizure <p>Muscle weakness : due to High K+</p> <p>Arrhythmias/ECG changes: due to \uparrow K+, \downarrow Ca+</p> <p>Seizure/tetany: due to low ca+</p> <p>Acute kidney injury: due to \uparrow Uric acid, \uparrow Phosphate Or calcium-phosphate crystal.</p>
<p>Key Concept of TLS = patients on combination chemotherapy for leukemia/lymphoma → arrhythmias, seizures, renal injury due to \uparrow K+, \uparrow PO₄⁻³, \downarrow Ca+ and \uparrow Uric acid. Treat with allopurinol or rasburicase- not together.</p>	

Langerhans cell histiocytosis	<p>Tumor of Langerhans cells, functionally immature cells, Presents in a child as lytic bone lesion/skin rash or recurrent otitis media with a mass on mastoid region.</p> <p>Tumor cells express S-100 + CD1a</p> <p>Birbeck granules – tennis racket/ rod shaped on EM are special features of this tumor.</p>
Hemophagocytic lymphohistocytosis	<p>Systemic overactivation of macrophages + cytotoxic T cells and \uparrow serum ferritin due to inherited defect or secondary to over activation of immune response (due to cancer or infection e.g EBV).</p> <p>Presents with pancytopenia, fever and hepatosplenomegaly.</p> <p>On bone marrow analysis: macrophages phagocytizing marrow elements are seen.</p>

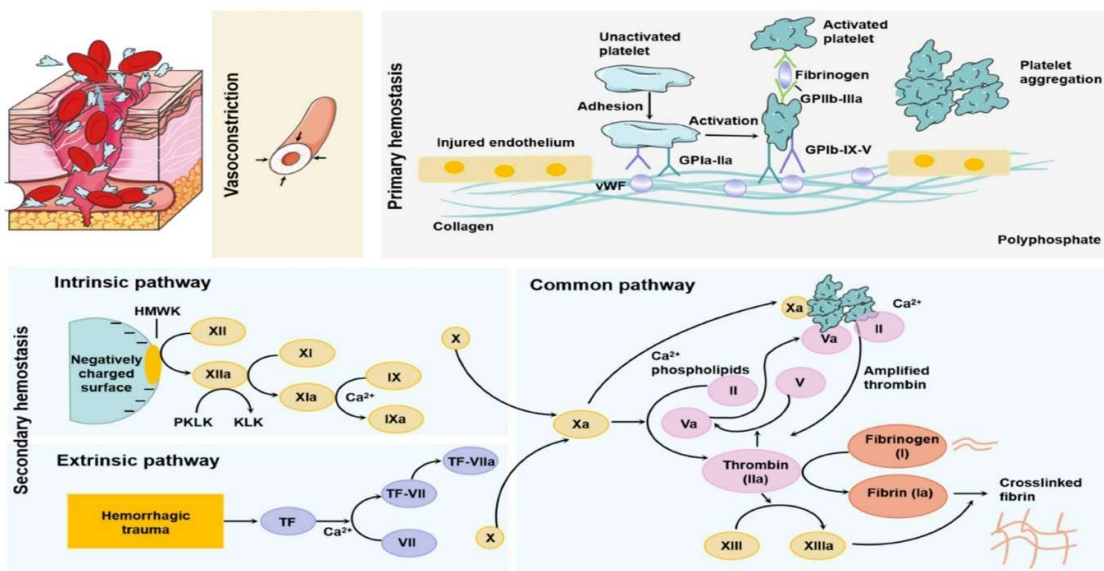
PLATELETS, COAGULATION CASCADE & THEIR DISORDERS

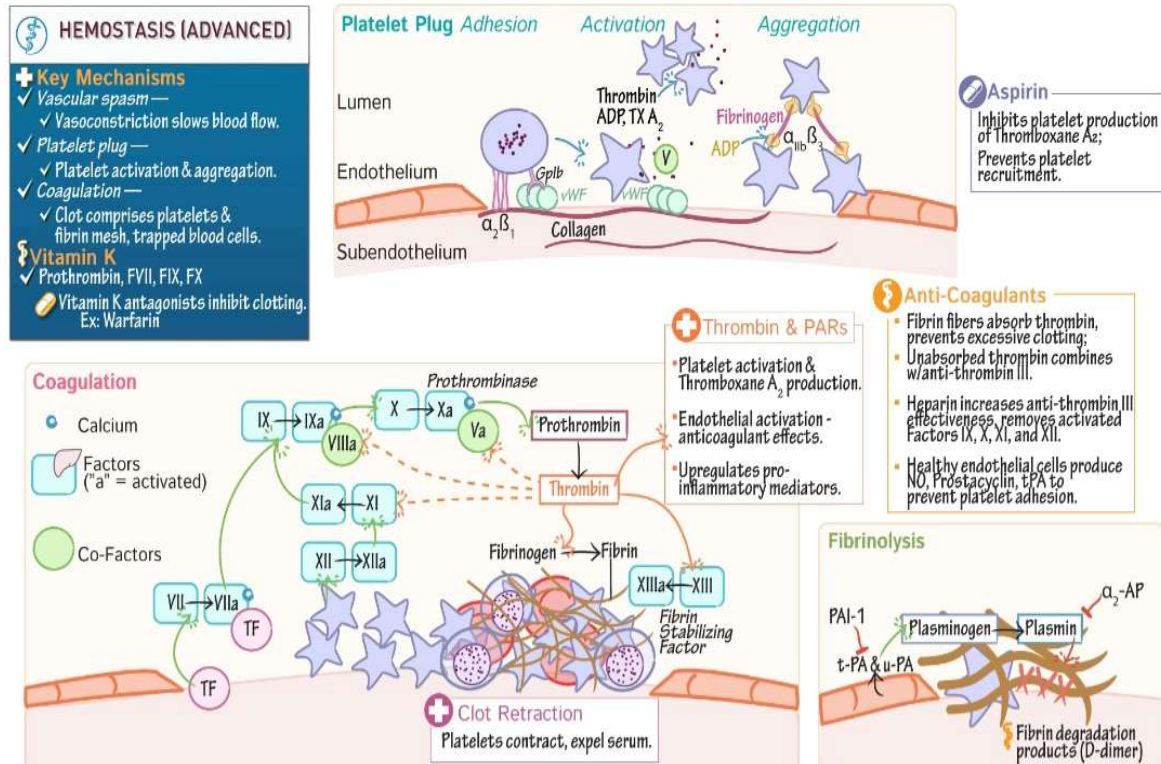
Thrombocytes (Platelets)

- Anucleate, Small Cytoplasmic fragments derived from Megakaryocytes. Normal count = $150 - 450 \times 10^9/L$
- Thrombopoietin stimulates megakaryocyte Proliferation.
- Approximately 1/3rd % of platelet pool is stored in The spleen (and they are not counted in Normal PLT count)
- Thrombocytopenia or decreased platelet function results in petechiae
- Life span of 8-10 days and involved in 1st hemostasis.
- When activated by endothelial injury, Aggregate with other platelets and interact With fibrinogen to form platelet plug, PLT Contain:
- Dense granules (Ca, ADP, Serotonin Histamine: CASH) and Alpha granules (WWF, Fibrinogen, fibronectin, platelet factor 4)
- Receptors On platelets: vWF receptor is Gplb and Fibrinogen receptor is Gpllb/IIla

Primary homeostasis	Secondary homeostasis
<p>Formation of initial platelet plug by interaction of blood vessel, vWF and platelets.</p> <p>Components: Endothelial Cells, platelets, adhesive Proteins including vWF and Collagen, and facilitators Including thrombin. Platelets changes shape from flat to round.</p> <p>Sequence of Events: Platelet adhesion, platelet Activation, and the platelet Plug formation</p> <p>Final Result: Formation of A platelet plug Serves as an immediate Response to the vascular Injury, limiting bleeding.</p>	<p>The cascade of reactions involving conversion of fibrinogen to fibrin monomers</p> <p>Components: Cells, Enzymatic and non-enzymatic Coagulation factors, Phosphatidylserine and Calcium</p> <p>Sequence of Events: Initiation of thrombin Generation, amplification Of thrombin generation. Propagation of thrombin Generation and fibrin Formation</p> <p>Final Result: Formation of a Stable, fibrin clot Produces a reinforcement effect on the platelet plug from fibrin thus Stabilizing it.</p>

- Aspirin irreversibly inhibits cyclooxygenase Thereby inhibiting TXA2 synthesis
- Clopidogrel, prasugrel, ticagrelor, and Ticlopidine inhibit ADP-induced expression of Gpllb/IIla by blocking P2Y₁ receptor
- Abciximab, eptifibatide, and tirofban inhibit Gpllb/IIla directly
- Ristocetin activates vWF to bind Gplb, Failure Of aggregation with ristocetin assay occurs in Von Willebrand disease and Bernard-Soulier Syndrome. vWF carries/protects factor VIII
- Desmopressin promotes the release Of WF and factor VIII from endothelial cells.





- **REGULATORY ANTICOAGULANT PROTEINS:** Proteins C and S
- **ANTICOAGULANTS:** Heparin, LMWH and Direct thrombin inhibitors (eg, argatroban, bivalirudin Dabigatran)
- **THROMBOLYTICS:** Alteplase, reteplase, Streptokinase, tenecteplase (tenecteplase > reteplase > Alteplase > Sk)
- **ANTIFIBRINOLYTICS:** Aminocaproic acid and Tranexamic acid

Vitamin K deficiency:

- dec. Synthesis of factors 2, 7, 9, 10, protein C and protein S.
- Warfarin inhibits vitamin K epoxide reductase.
- Vitamin K administration can potentially Reverse inhibitory effect of warfarin on clotting
- Factor synthesis (delayed).
- FFP or PCC Administration reverses action of warfarin Immediately can be given with vitamin K In cases of severe bleeding
- Neonates lack enteric bacteria, which produce Vitamin K. Early administration of vitamin K Overcomes neonatal deficiency/coagulopathy
- Factor VII (seven)-shortest half-life and Factor II (two)—longest (too long) half-life
- Antithrombin inhibits thrombin (factor IIa) + factor Xa mainly but it also inhibits Factors VII, IX, XI, XII.
- Heparin enhances the activity of Antithrombin.
- Factor V Leiden mutation produces a factor V Resistant to inhibition by activated protein C.
- tPA is used clinically as a thrombolytic

IMP CONCEPTS:

- For immediate/early reversal of warfarin action → use FFP. For delayed reversal of warfarin action → use Vit K
- IN severe bleeding → FFP + Vit K
- Protein C & S inhibit Factors Va (5) and XIIIa (8). Memorize by CS – 58)

Bleeding time (BT normal 2-7 min)	Clotting time (CT normal 8-15 min)	Prothrombin time (PT normal 10-14 sec)	Activated partial thromboplastin time (aPTT 25-36 sec)
Time taken for a skin puncture to stop bleeding. BT is an indicator Of platelet plug formation (primary hemostasis) Prolonged bleeding time is an indicator of Low platelet count Or vWF deficiency or PLT functional defects.	Time taken for the formation of the stable fibrin. Prolonged CT indicates defects in the coagulation pathway (secondary hemostasis) Specific defects of the intrinsic/ extrinsic pathways are indicated by PT / APTT	Tests the function of common pathway + extrinsic pathway. Factors 1,2,5,7,10 INR= Pt.PT/Control PT Normal = 1 >1 is prolonged INR. Used to assess pts on warfarin.	Tests the function of common + intrinsic pathway. All Factors except 7, 13. ↑ APTT seen in Haemophilia ↑ BT, ↑ aPTT in wVD.

PLATELET DISORDERS

- Present with petechial cutaneous bleeding or mucosal bleeding.
- All platelet disorders have increased bleeding time (BT) due to low PLT count.
- But functional or qualitative disorders of PLT have normal PLT count

Immune
thrombocytopenia
(ITP)

- **Primary:** isolated thrombocytopenia (platelet count < 100x10⁹/L) with no other cause of Thrombocytopenia i.e idiopathic.
- **Secondary:** thrombocytopenia associated with another condition (e.g. HIV, HCV, SLE, CLL)
- **Drug-induced:** drug-dependent platelet antibodies causing platelet destruction e.g Heparin, thiazide diuretics, Rifampin etc.
- **Types**
- **Childhood ITP:** 2-6 yr of age, history of Recent Viral Infection, including Varicella Zoster or Measles. Spontaneous Remission is 80% or More
- **Adult ITP:** age 20-40 yr, rare remission, more in females –F > M (3:1), Mostly idiopathic.
- although it can be associated with Connective tissue disease (such as SLE).
- Lymphoproliferative disease (such as lymphoma)
- Medications and Infections (such as hepatitis C virus and HIV Infections).
- HCV → cirrhosis-related splenomegaly
- HIV → direct suppression of platelet production
- **Pathogenesis:** destruction of platelets in spleen by splenic macrophages due to auto antibodies to GpIIb/IIIa. Primary ITP is idiopathic so the term used idiopathic thrombocytopenic Purpura.
- **Clinical features:** Purpura/rash, easy bruising, epistaxis/menorrhagia. Splenomegaly is rare or absent. Rest all examination is normal.
- **Investigations:**
- CBC: Low platelet count, when count falls to 20K – risk of severe and spontaneous bleeding.
- PT/APTT are normal. BT is prolonged.
- Peripheral smear: Giant platelets.
- Bone marrow examination: Hypercellularity (↑ megakaryocytes and megakaryopoiesis)
- **Treatment:** Steroid, IVIG, Rituximab, TPO agonists (eltrombopag), splenectomy – refractory cases and unresponsive to drugs.
- A patient pt. Presents with bleeding and petechial rash, her PLT = 5000k , prior treatment compromised of steroids but no response, what will be management keeping in mind the diagnosis of ITP → IVIG (not splenectomy) – Past paper BCQ

Bernard-Soulier
syndrome

- Autosomal recessive disorder, lack of GpIb → defective vWF to platelet adhesion.
- So basically BSS is a disorder of defective adhesion → abnormal ristocetin test.
- CBC shows low PLT count, but mildly low platelets (unlike ITP)
- Peripheral smear and bone marrow exam show large/ giant platelets. BT – prolonged.
- Platelet flow cytometry confirms the diagnosis.

NOTE:

- Both ITP and BSS have low PLT count , giant platelets and ↑ megakaryopoiesis, ↑ BT
- The difference lies in PLT count. If mildly low → BSS, If severely low → ITP

Glanzmann thrombasthenia	<ul style="list-style-type: none"> Autosomal recessive disorder leads to ↓ GpIIb/IIIa → defective aggregation and impaired platelet plug formation. Blood smear shows no platelet clumping. CBS shows Normal PLT count. BT is prolonged. Platelet flow cytometry confirms the diagnosis.
Gestational thrombocytopenia	<ul style="list-style-type: none"> Benign, mild thrombocytopenia in 3rd trimester of pregnancy. Usually resolves after delivery. Platelet count is does not go beyond 60 – 70K.
Thrombotic thrombocytopenic Purpura	Hemolytic-Uremic syndrome
<ul style="list-style-type: none"> Deficiency of VWF metalloprotease (ADAMTS 13) leads to accumulation of vWF multimers → ↑ PLT adhesion and aggregation. Mostly middle-aged female patient presents triad of Microangiopathic hemolytic anemia + Low PLT + neurological symptoms. Fever is also present. Schistocytes on peripheral smear PT/ APTT, fibrinogen → all normal. Plasma exchange with steroids is the dependant modality of treatment. Rituximab may be used 	<ul style="list-style-type: none"> Mostly in children, presents with triad of: microangiopathic HA + Diarrhea + Renal failure. Shiga toxin → E.coli serotype O157 : H7 is the cause. -ve Coombs test in both HUS and TTP. Normal coagulation profile: PT/APTT in both. RFTs deranged in HUS. Low PLT count + schistocytes on peripheral smear. Supportive treatment only. Avoid PLT transfusion in both HUS & TTP

DISORDERS OF COAGULATION

- Basically, they are disorders of secondary hemostasis. Coagulation profile – PT/aPTT is deranged.
- Coagulation disorders can be due to clotting factor deficiencies or acquired factor inhibitors (most Commonly against factor VIII). Diagnosed with a mixing study, in which normal plasma is added to patient's plasma.
- Clotting factor deficiencies should correct (the PT or PTT returns to within the appropriate normal range), whereas factor inhibitors will not correct.
- Coagulation Disorders include Haemophilia (intrinsic pathway defect) or Vit K def. (General coagulation defect)
- Mixed Platelet + coagulation disorders → vWD and DIC.

Hemophilia	<ul style="list-style-type: none"> Intrinsic pathway coagulation defect (↑ PTT or aPTT) Hemophilia A: deficiency of factor VIII (minor component) ; X-linked recessive. Hemophilia B: deficiency of factor IX; X-linked recessive. Hemophilia C: deficiency of factor XI; autosomal recessive. Hemorrhage in Hemophilia → hemarthroses (bleeding into joints (knee) Easy bruising, bleeding after trauma or surgery (eg, dental procedures) Treatment: Desmopressin, factor VIII concentrate, emicizumab (A) factor IX Concentrate (B); factor XI concentrate (C).
Von Willebrand disease	<ul style="list-style-type: none"> Mild, but most common inherited bleeding disorder/coagulopathy. Mostly autosomal dominant Intrinsic pathway defect – raised aPTT. Defect in PLT to vWF adhesion. Role of von Willebrand factor: Large glycoprotein which forms massive multimers up to 1,000,000 Da in size, Promotes platelet adhesion to damaged endothelium Carrier molecule for factor VIII. Types Type 1: partial reduction in vWF (80% of patients) Type 2: abnormal form of vWF Type 3: total lack of vWF (autosomal recessive) Investigation: Prolonged bleeding time, APTT may be prolonged Factor VIII levels may be moderately reduced (major component of factor VIII). Defective platelet aggregation with ristocetin -- abnormal ristocetin test. Management Tranexamic acid for mild bleeding Desmopressin (DDAVP): raises levels of VWF by inducing release of VWF from Weibel-Palade Bodies of endothelium
Disseminated intravascular coagulation	<ul style="list-style-type: none"> The processes of coagulation and fibrinolysis are dysregulated, and the result is widespread Clotting with resultant bleeding, Regardless of the triggering event of DIC, once initiated, the Pathophysiology of DIC is similar.

	<ul style="list-style-type: none"> Trauma, sepsis, snake bite, obstetric complications, acute pancreatitis, malignancy, or transfusion → release of tissue factor/ Thromboplastin → TF (factor III) contacts with general circulation, activation of widespread coagulation cascade leads to consumption of clotting factors → Bleeding. So, first thrombosis occurs followed by bleeding event. Investigations: Schistocytes on peripheral smear (in DIC, HUS, TTP, HELLP syndrome). Specific test: D – Dimers raised; sensitivity is high for → increased fibrin degradation products). ↓ fibrinogen, ↓ factor 5,8 (58), low platelet count, ↑ BT, PT, aPTT (all raised).
Vit. K deficiency	<ul style="list-style-type: none"> General coagulation defect, Bleeding time normal, ↑ PT, ↑ aPTT Decreased activity of factors I, VII, IX, X, protein C, protein S. Neonates lack Vit k due to sterile gut, must be given Inj Vit K 0.5mg IV Liver disease/Vit K def. Both present with raised PT & APTT.

Hemostatic Changes in Pregnancy		
Remains same	Increased	Decreased
<ul style="list-style-type: none"> Factor II, V, IX Protein C Anti-thrombin III 	<ul style="list-style-type: none"> vWF raised, factors VII, VIII, fibrinogen Plasminogen activator inhibitor 1, 2 Plasminogen Resistance to activated protein C D - dimers 	<ul style="list-style-type: none"> Protein S Factor XI
Pregnancy is mainly a Hyper coagulant/pro-coagulant/ thrombotic state.		

THROMBOPHILIAS	
<ul style="list-style-type: none"> They May be inherited/acquired, mostly are inherited. All inherited thrombophilias are autosomal dominant and lead to hypercoagulable state. Hereditary thrombophilias include Factor V Laden mutation, protein C/S deficiency, AT III deficiency, prothrombin gene mutation. Most common inherited thrombophilia is Factor V laden mutation and MC acquired is antiphospholipid syndrome 	
Anti thrombin III deficiency	<ul style="list-style-type: none"> Has no direct effect on the PT, PTT, or thrombin time but diminishes the increase in PTT following standard heparin dosing. Can also be acquired: renal failure/nephrotic syndrome - Antithrombin loss in urine → dec. inhibition of factors IIa and Xa.
Factor V Laden mutation	<ul style="list-style-type: none"> Production of mutant factor V (guanine → adenine DNA point mutation That mutant factor V is resistant to degradation by activated protein C. Complications include DVT, cerebral vein thrombosis, recurrent pregnancy loss
Protein C/S deficiency	<ul style="list-style-type: none"> It leads to decreased ability to inactivate factors Va and VIIIa. Increased risk of warfarin induced skin necrosis
Prothrombin gene mutation	<ul style="list-style-type: none"> Point mutation in 3' untranslated region → Raised production of prothrombin and plasma levels leads to venous thrombosis.
Antiphospholipid antibody syndrome	<ul style="list-style-type: none"> Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thrombosis, recurrent fetal loss, and thrombocytopenia. It may occur as a primary Disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE) In pregnancy the following complications may occur: Recurrent miscarriage, IUGR, Pre-eclampsia, Placental abruption, Pre-term delivery and Venous thromboembolism Diagnosis is based on clinical criteria including history of thrombosis (arterial or venous Or spontaneous abortion along with laboratory findings Lab findings: lupus anticoagulant (raised aPTT), anticardiolipin antibody, anti-B2 Glycoprotein antibodies Management Low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing Low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually Discontinued at 34 weeks gestation. These Interventions increase the live birth rate 7-fold.

Condition	Platelet Count	Bleeding Time	PT	PTT
Hemophilia	NL ^a	NL	NL	Increased
vWD	NL	Increased	NL	Increased
ITP	Decreased	Increased	NL	NL
TTP	Decreased	Increased	NL	NL
DIC	Decreased	Increased	Increased	Increased
Heparin	NL or decreased	NL	NL	Increased
Warfarin	NL	NL	Increased	NL
Liver disease	NL	NL	Increased	Increased

^aNL = normal.

For ITP

- No bleeding, count >30,000 → No treatment
- Mild bleeding, count <30,000 → Steroids
- Severe bleeding (GI/CNS), count < 10,000 → IVIG, Anti -Rho (Anti-D)
- Recurrent episodes, steroid dependent → splenectomy
- Splenectomy or steroids not effective → Rituximab, cyclosporine, azathioprine, eltrombopag, mycophenolate.

BLOOD & BLOOD PRODUCTS – FFP, PCC, CPP

Packed RBCs are indicated in acute blood loss and severe anemia (Hb < 7mg/dL).

Give FFP in factor IX deficiency and CPP in factor VIII deficiency (Hemophilia A)

Fresh frozen plasma (FFP)	Cryoprecipitate (CPP)	Prothrombin complex concentrate (PCC)	CMV Negative and Irradiated blood
<p>It increases coagulation factors levels. Generally contains all coagulation factors and plasma proteins.</p> <p>Most suited for 'clinically significant but without 'major haemorrhage' in patients with a (PT) ratio or (APTT) ratio > 1.5.</p> <p>Typically 150-220 mL Can be used prophylactically in patients undergoing invasive surgery where there is a risk of Significant bleeding. Used for immediate reversal of warfarin toxicity and liver cirrhosis.</p> <p>In contrast to red cells, the universal donor of FFP is AB</p>	<p>Contains concentrated Factor VIII, von Willebrand factor, fibrinogen, Factor XIII, fibronectin. (1,8,13,vWF)</p> <p>CPP produced by further processing of Fresh Frozen Plasma (FFP)</p> <p>Clinically it is most Commonly used to replace fibrinogen</p> <p>Much smaller volume than FFP, typically 15-20mL</p> <p>Most suited for patients for clinically significant" but without major hemorrhage who have a Fibrinogen concentration < 1.5 g/L</p> <p>Example- use cases include disseminated intravascular</p>	<p>PCC Contains factor II, VII, IX, X, protein C and S.</p> <p>Used for the emergency reversal of anticoagulation in patients with either severe bleeding or a Head injury with suspected intracerebral haemorrhage</p> <p>PCC can be used prophylactically in patients undergoing emergency surgery depending on the circumstance</p>	<p>Cytomegalovirus (CMV) is transmitted in leucocytes. As most blood products (except granulocyte</p> <p>Transfusions) are now leucocyte depleted CMV negative products are rarely required</p> <p>Irradiated blood products are used to avoid transfusion graft versus host disease (TA-GVHD) caused By engraftment of viable donor T lymphocytes.</p> <p>Most common + lethal infection transmitted via blood is CMV.</p>

blood because it lacks any anti-A or anti-B antibodies	coagulation, liver failure and Hypofibrinogenaemia secondary to massive transfusion. It may also be used in an emergency Situation for haemophiliacs when specific factors not available, and in von Willebrand disease Can be used prophylactically in patients undergoing invasive surgery where there is a risk of Significant bleeding where the fibrinogen concentration < 1.0 g/L		
Platelets Transfusion --Active Bleeding			
<p>It should be noted that platelet transfusions have the highest risk of bacterial contamination Compared to other types of blood product.</p> <p>Offer platelet transfusions to patients with a platelet count of $<30 \times 10^9$ with clinically significant Bleeding (melena)</p> <p>Platelet thresholds for transfusion are higher (maximum $< 100 \times 10^9$) for patients with severe Bleeding or bleeding at critical sites, such as the CNS</p> <p>Pre-invasive procedure (prophylactic)</p> <p>Platelet transfusion for thrombocytopenia before surgery/ an invasive procedure. Aim for pit levels Of: 50×10^9/ for most patients, $50-75 \times 10^9$/L if high risk of bleeding, 100×10^9/L if surgery at critical site</p> <p>If no active bleeding or planned invasive procedure A threshold of 10×10^9 except where platelet transfusion is contraindicated or there are Alternative treatments for their condition</p> <p>For example, do not perform platelet transfusion for any of the following conditions: Chronic bone marrow failure and Autoimmune thrombocytopenia</p>			

HEPARIN	WARFARIN
<ul style="list-style-type: none"> Given parenteral (IV/SC), acts on blood Rapid Onset of action (seconds) Mech: activates AT III → decreases action of factor IIa, Xa Duration of action (hours), cleared by liver. Doesn't cross placenta Monitored by PTT (intrinsic pathway) Effect reversed by protamine sulphate. Side effects include Bleeding, osteoporosis, thrombocytopenia. LMVH: enoxaparin, dalteprin → act on factor Xa mainly. Undergo renal clearance, use with caution in renal insufficiency. Effect is not easily reversible Fondaparinux- acts only on factor Xa. Longer half life 2 to 4 times than Unfractionated/HMWH and better bioavailability 	<ul style="list-style-type: none"> Given Orally, acts on Liver Slow Onset of action, required for chronic anticoagulation. Mech: inhibits Vit K epoxide reductase (VKOR) – inhibition of Vit K dependant gamma carboxylation of factors 2,7,9,10 and protein C & S. Duration of action (days) crosses placenta – teratogenic Monitored by INR > PT (extrinsic pathway) Effect reversed by Vit K (slow), FFP (rapid reversal). Side effects: initial risk of hypercoagulation, skin/tissue necrosis. Initial heparin therapy reduces the risk of recurrent DVT/skin necrosis.
<ul style="list-style-type: none"> Heparin induced Thrombocytopenia type 1: Non-immune mediated, mild dec in PLT (>1 lac), Occurs within 2 days of treatment, not clinically significant so continue treatment. HIT – Type 2: highest risk with high mol. weight heparin 	<ul style="list-style-type: none"> Direct coagulation factors inhibitors They do not require Lab monitoring Bivalirudin – inhibits thrombin (IIa) Dabigatran (oral) – inhibits IIa Apixaban, endoxaban – inhibit factor Xa, given orally.

<ul style="list-style-type: none"> • Autoantibodies against heparin bound platelet factor 4. • Ab- heparin PF4 complex binds and activates PLT, removal by splenic macrophages. • PLT fall < 60000/uL • Risk of thrombosis, discontinue heparin and use alternate anticoagulants. 	<p>Reversal of action:</p> <ul style="list-style-type: none"> ○ Dabigatran reversal by monoclonal Ab (idarucizumab) ○ Direct Xa inhibitors reversal by recombinant modified inactive factor Xa → Andexanet Alfa
ANTI PLATELETS	THROMBOLYTICS
<ul style="list-style-type: none"> ❖ Inhibit platelet aggregation. ❖ Aspirin → irreversibly blocks COX I,II → 1 TXA2 ❖ Given in Acute coronary syndrome. ❖ Clopidogrel → block ADP (P2Y12) receptor. Used with aspirin in ACS ❖ Abciximab/tirofiban → block GpIIb/IIIa on activated PLT. Used in unstable angina and PCI ❖ Cilostazol/Dipyridamole → block PDE – dec cAMP in PLT ❖ Used in prevention of coronary stent restenosis, intermittent claudication 	<ul style="list-style-type: none"> ❖ Alteplase, reteplase, streptokinase, tenecteplase. ❖ Directly/indirectly convert plasminogen → plasmin. ❖ Which cleaves fibrin and thrombin clots. ❖ They inc. PT/APTT, no effect on PLT count. ❖ Used in early MI, early stroke – within 2 hrs , severe PE. ❖ Side effects: Bleeding ❖ Contraindicated in active bleed, recent surgery or history of intracranial bleed ❖ Reversal with Tranexamic acid, Aminocaproic acid, platelets transfusion, FFP, CPP/ PCC.

Amelioration of Adverse effects of Chemotherapy (Rescue Therapy)

Drug & Mechanism	Clinical use
Leucovorin (folinic acid) – tetrahydrofolate precursor	Myelosuppression from methotrexate
Ondansetron – 5HT3 antagonist	Chemotherapy induced vomiting (1 – 2 hrs)
Aprepitant – NK1 receptor antagonist	Chemotherapy induced vomiting >24 hrs.
Metoclopramide/prochlorperazine – D2 Antagonist	
Filgrastim – recombinant GM - CSF	Neutropenia
Epoetin alpha – Recombinant EPO	Anemia (CKD) given Sub cut.
Mesna	Hemorrhagic cystitis from cyclophosphamide
Dexrazoxane – iron chelator	Cardiotoxicity from anthracyclins
Amifostine – free radical scavenger	Nephrotoxicity from platinum compounds
Rasburicase – catlyzes uric acid → allantoin	Tumor lysis syndrome

CHEMOTHERAPY PRINCIPLES

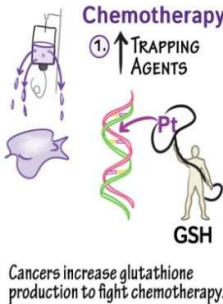
Principles

- ✓ TERMINOLOGY
- ✓ MECHANISMS
- ✓ RESISTANCE

Terminology

Log-Kill Hypothesis
Chemotherapy kills a constant fraction of cells.

Clinical Settings
PRIMARY (INDUCTION)
First-line chemotherapy.
NEOADJUVANT
Chemotherapy to shrink tumor size.
ADJUVANT
Additional chemotherapy to prevent recurrence.

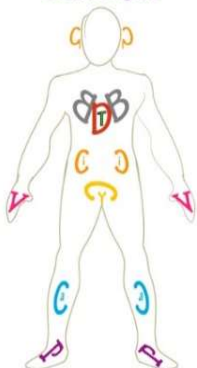


CHEMOTHERAPY SIDE EFFECTS

Side Effects

- ✓ HIGH YIELD SIDE EFFECTS
- ✓ COMMON CLINICAL EFFECTS

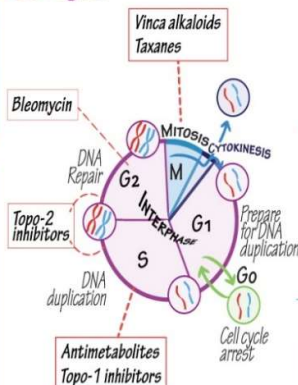
Chemo Figure



- C₁ Cisplatin – Oto- & Nephrotoxicity
- C₂ Carboplatin – Myelosuppression
- B Bleomycin – Pulmonary fibrosis
- D, T Doxorubicin, Trastuzumab – Heart failure
- C₃ Cyclophosphamide – Hemorrhagic cystitis
- V, P Vincristine, Paclitaxel – Neuropathy

Chemotherapy Mechanisms

Cell Cycle



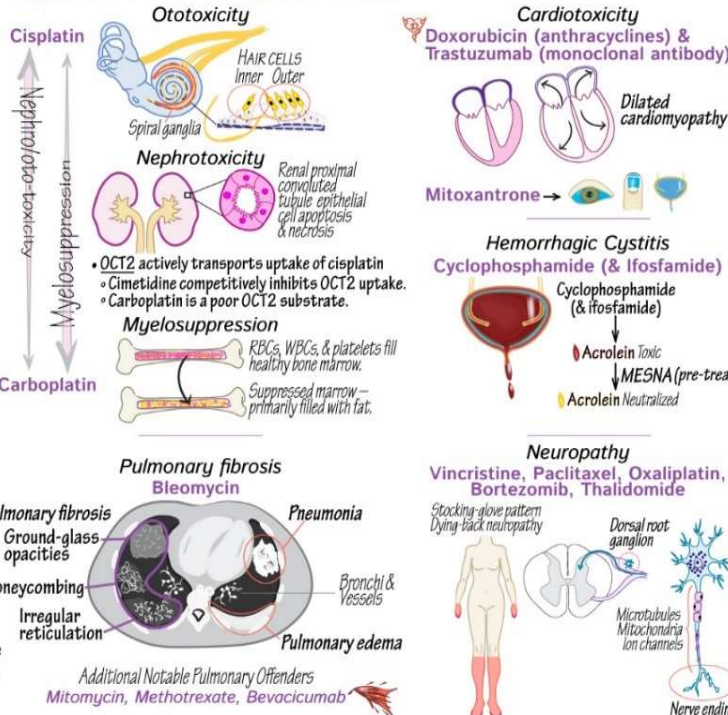
Cell-Cycle Specific (CCS)

- S** **ANTIMETABOLITES**
 - Methotrexate, 5-Fluorouracil, 6-Mercaptopurine, Cytarabine (Ara-C)
 - Topoisomerase I inhibitors**: Topotecan, Irinotecan (Camptothecins)
 - Topoisomerase II inhibitors**: Etoposide, Teniposide (Podophyllotoxins)
- G₂** **ANTITUMOR ANTIBIOTIC**
 - Bleomycin
- M** **MICROTUBULE INHIBITORS**
 - VINCA ALKALOIDS**: Vincristine, Vinblastine
 - TAXANES**: Paclitaxel

Cell-Cycle Nonspecific (Any phase)

- CLASSIC**
 - NITROGEN MUSTARDS**: Cyclophosphamide, Chlorambucil
 - NITROSOUREAS**: Lomustine, Carmustine
 - HYDRAZINES & TRIAZINES**: Procarbazine, Dacarbazine
 - TEMOSOLIMIDE** (Gliomas): Temozolomide
- NON-CLASSIC**
 - PLATINUM ANALOGS**: Cisplatin, Carboplatin, Oxaliplatin
 - ANTHRACYCLINES**: Doxorubicin, Daunorubicin, Mitoxantrone
 - MISCELLANEOUS**: Mitomycin
- PROTEIN KINASE INHIBITORS**: Imatinib (Tyr) (CML)
- MONOCLONAL ANTIBODIES**: Trastuzumab (HER2), Bevacizumab (VEGF), Rituximab (B lymph)
- PROTEASOME INHIBITORS**: Bortezomib (Myeloma)
- HORMONES**: Glucocorticoids, Estrogens
- HORMONE ANTAGONISTS**: Tamoxifen (Breast), Flutamide (Prostate)
- MISCELLANEOUS**: Thalidomide

High Yield Chemotherapy Side Effects



COMMON SIDE EFFECTS

- Constitutional**
 - Fatigue
 - ↓ Appetite
 - ↓ Weight
 - ↓ Libido
- Gastrointestinal**
 - Nausea/Vomiting
 - Constipation
 - Diarrhea
- Dermatologic**
 - Mucositis
 - Rash
 - Alopecia (hair loss)
 - Dry skin/nail changes
- Neurological/Psychiatric**
 - Chemo brain
 - ↓ Memory & Concentration
 - Mood changes
 - Neuropathy
- Obstetrics**
 - Infertility
 - Teratogenicity
- Genitourinary**
 - Cystitis
 - Pain (dysuria)
 - Frequency/Urgency
 - Hesitancy

PAST PAPERS BCQs

1. Which of the following is the most common inherited bleeding disorder (coagulopathy) = VWD.
2. Treatment of Erythroblastosis fetalis of B+ Exchange transfusion done with which of following = B-ve.
3. Lady with hypochromic microcytic anemia HBA 96 % HBA2.4 what is your diagnosis = Thalassemia minor
4. The maturation of T cells occurs in = Thymus.
5. A pregnant lady in 33 weeks taking only iron supplements she will be deficient in = Calcium > Folic acid.
6. Young girl oral bleeding, gingival swelling, petechiae, lower lip paraesthesia, CBC and bone marrow biopsy advised. Which is most likely diagnosis = Leukemia.
7. ALL marker is = CD 10 (pre-B cells)
8. After gastrectomy which type anaemia occurs commonly = Iron deficiency anemia.
9. partial gastrectomy has been done which type of anaemia occurs = Microcytic hypochromic anaemia (Fe def)
10. ABGs samples collected in = Whole arterial blood in heparinized syringe.
11. Female patient presents with fever and excess menstrual blood loss her labs show HB Much less than her age and sex rang but ferritin is normal. What is conclusion = Concomitant sideroblastic anemia.
12. HB binds with which of following = Heptoglobin, whereas heme binds Hemopexin.
13. Venous blood is higher to arterial blood in = Hematocrit.
14. Clotting factor associated with prothrombin time are = 1,2,5,7,10.
15. Female presented with pallor fatigue and severe loss of vibration investigation of choice will be = B12 level.
16. Hemagglutinin feature is = Complex glycoprotein.
17. 11 years old child with bruises and occasional epistaxis sine birth, bleeding time is increased while platelets are 210000 , HB 12 What is the underlying defect = Platelet functional defect.
18. Patient presented with jaundice bilirubin 8 direct bilirubin 0.9 reticulocyte 10 ALT 17 ALP 75 Hb 7 combs test +ve what is likely cause = Hemolytic anemia.
19. A patient having bleeding tendency and diagnosed as VWD. Which among the following test is used for diagnosis of VWD disease = Increase BT (aPTT also raised) but BT is more specific for vWD.
20. Anti sera agglutinates with A and D and plasma has anti B antibodies which blood group it is = A+ve.
21. 18 years old boy came from KPK with painful legs, ulcers on the leg and mild jaundice. What is the probable diagnosis = Sick cell anemia.
22. A patient of VWD present with bleeding what is the most appropriate treatment of VWD if no factor 8 is available = Cryoprecipitate.
23. A girl with swollen tender knee history of excessive bleeding after tooth extraction. What is the suitable test for diagnose the cause of bleed = BT (more chances of vWD in females as compared to Hemophilia, so check BT)
24. Patient with Hb 6g/dl, enlarged spleen and recurrent blood transfusion, what's the diagnosis = Thalassemia major.
25. Anticoagulant released in blood by mast cells = Heparin.
26. Total hematocrit in infant is = 55. Blood clot consists of = Fibrin.
27. A 8 yr old boy with uneventful tooth extraction presented with very next day with bleeding likely reason is = Anti coagulant effect.
28. Most common inherited thrombotic disorder is = Factor V Leiden mutation (alone factor V def. Causes bleeding).
29. Insoluble form of iron stored is = Hemosiderin.
30. MCV remains normal in which = Acute blood loss for 2 days
31. A 9 years old boy with swollen tender knee, history of excessive after tooth extraction. What is the best test for diagnose cause of bleed = Factor 8 minor assays. (Hemophilia – factor 8 minor, vWD – factor 8 major)
32. A 20 years old lady who is 5 months pregnant complains of generalized weakness and lethargy her Hb is 9.8 g/dl with MCV 70 fl and MCH 15 pg. her serum ferritin level is 150 mg /dl, diagnosis is = Thalassemia trait. (normal ferritin)
33. A young boy having mass in neck biopsy of lymph node shows effaces architecture atypical mononucleosis cell with bilobed nucleus and eosinophilia and CD 15 and CD 30 positive diagnose is = Hodgkin lymphoma.(mixed cellularity)
34. An old man who was being treated by a GP for infection with certain drugs comes to you with complaints of generalized weakness, pallor, easy bruising. Hb 7g/dl and decrease RBC, WBC PLT. Retic count 0.1%. bone marrow exam shows hypocellular bone marrow with few cells, likely diagnosis is = Aplastic anemia.
35. What is the inheritance pattern of Hemophilia A = X linked recessive.(affects Males more)
36. O-ve blood transfused with AB+ve what is the secondary blood transfusion reaction = Hemoglobinuria.
37. A 6 months old baby fell from bed and got frontal ecchymosis his Hb is 6, platelets are 180k, sisters are normal but brother died of profuse bleeding after circumcision the most appropriate test to rule the cause = Coagulation profile.

38. A 45 years man complains of lethargy, worse after he takes a hot shower. He also says that he feels a burning sensation in his fingers and toes. Splenomegaly was found. His medical history reveals gout. RBC, WBC and platelets raised and erythropoietin decrease what is the single most likely diagnosis = Polycythaemia rubra Vera (PRV).
39. A patient is having bleeding problem lab shows PT 14sec, APTT 50sec (prolonged) bleeding time 5mins, defect in which of following pathway = Intrinsic pathway (APTT raised only)
40. International normalized ratio INR is use for = Monitoring of Oral anti coagulants therapy (warfarin)
41. 21 years old boy diagnosed with leukemia he has to undergo bone marrow biopsy patient bone marrow is taken from which of following = Sternum. (Prefer ventral iliac crest, the suitable given option in exam was sternum).
42. Chronic intravascular hemolysis is characterized by = Hemosiderinuria.
43. A lady taking rheumatoid arthritis drugs presents with weakness and malaise. Her retic count 0.1 % HB 8, WBC 2x10 and platelets 200K, bone marrow is hypercellular likely cause is = Megaloblastic anemia.
44. Regarding lymphocytes true is = Are cancer fighting cells.
45. pale lethargic lady deprived of ante natal care, during delivery she bleeding heavily which nutrient deficiency = Iron.
46. Diagnostic of iron deficiency anemia is by = Serum ferritin (also do it for diagnosing IDA in pregnancy)
47. A pale and lethargic boy, her mother elaborate history of eating mud (pica) what is the underlying cause of eating these deficiency.= Iron deficiency (related to non-nutritious intake/Pica intake)
48. In hemostasis the word gain is for = Exaggeration of the clotting mechanism.
49. A 19 years old female feeling lethargy and irritability for 5 year presents to you. Her Hb is 9, MCV 65, MCHC low WBC and platelet count normal. Two months after taking iron supplements her Hb was 10.2 How will you confirm the cause of continuity of her anemia = HB Electrophoresis (Hb didn't improve significantly after Fe – do Hb – electroph)
50. A male noticed some skin nodules ranging from 1 to 2mm in size, there was a lesion in brain upon doing CT scan and also some lesion in the abdomen was noticed with CT, What's the mutation involved in the disease = NF 1
51. Patient undergoes gastrectomy develop macrocytic anemia treatment should be? Injection Vit. B12. (IM)
52. A 30 years boy develops jaundice, pallor, and breathlessness having and again likely cause = Hemolytic anemia.
53. Lady had a difficult labour at home in village. She was brought to hospital. Her Hb 5g/dl, platelets 20K, TLC 2400 with Neutrophilia, the peripheral film shows burr cells. Her PT & APTT were prolonged. Most likely cause is = DIC.
54. A 45 year man presented with Hb 8, enlarged spleen. WBC raised. Peripheral smear showing immature myeloid lineage. What is the genetic defect = 9:22 (CML)
55. Regarding haematopoiesis true is = 75% myeloid stem cells.
56. A 50 year patient presents with jaundice. On workup HB 6 g/dL, increase bilirubin, increase retic count 4%, smear show polychromasia and clumps, what test to confirm diagnosis = Coombs test.
57. A patient of arthritis using drugs for 06 months presents with HB 10 g/dL, MCV 105fl, MCH=31, bone marrow biopsy show hyper cellular = Megaloblastic anemia.
58. A 22 years man with sore throat & cervical lymphadenopathy; CBC picture shows presence of atypical lymphocytes the most important test in this setting is = Monospot test.
59. After mismatched blood transfusion what will occur = Donor blood agglutinated and hemolysis.
60. Normal physiological parameters of blood components or cells are = 45% blood cells and 55 % plasma.
61. A young female presented with lethargy gum bleeding, anemia petechiae, best for diagnose = Bone marrow biopsy.
62. A female patient with Hb 9.8 g/d; and doctor prescribed iron, after 2 months she presents with Hb 10.2 g/dl. What should r further considered for diagnosis = Hb electrophoresis. (Hb didn't improve significantly so do Hb-electroph.)
63. A 16 yr. male presented to OPD with 102 F fever for last 4 days and gives history of using Anti-malarial she has been passing cola color urine with deranged LFTs and increased unconjugated bilirubin. What is the cause = G6PD def.
64. Bone marrow biopsy is done at which of following site = Ventral iliac crest.
65. Which of the following is last to appear normal in blood after hemorrhage = RBCs.
66. A soldier after returning from siachin, having spent 6 months there, presents to CMH Skardu with complains of headache and peripheral cyanosis of his fingers. Most probably the cause is = Secondary Polycythemia.
67. Aplastic anemia characteristic feature is = Fatty marrow.
68. A boy after RTA losses 2 liters blood what type of anemia will be there = Normochromic normocytic anemia.
69. Mother Rh + Ve & father is Rh – Ve what's the risk = No risk > Rh antigen will leak into mother.
70. The blood group antigens are not present on RBCs until = 20 Weeks.
71. A 15 year old girl presented with epistaxis and ecchymosis on bone marrow aspirate, there is hyperplasia of megakaryocytes, the most likely diagnosis is = ITP.
72. A female present with fatigue, easy bruisability after small cut and recurrent infection alongside fever from 3 weeks. After investigations the report shows blast cells and Promyelocyte in smear. Suspected Diagnose is indicated by which translocation = t 15:17 (AML, M3)

73. Most common presentation of G6PD is = Infection related hemolysis > Acute drug induced hemolysis.
74. 59year old patient with generalized lymphadenopathy. Platelets and TLC count was raised. Peripheral smear showed mature lymphocytes. What is the diagnosis = CLL .
75. Which test is diagnostic for pernicious anemia = Anti intrinsic factor antibodies.
76. A thalassemic child took appointment from dentist for tooth extraction but two days before that he developed deep jaundice dark urine HB 4.9, MCV 56 hepatosplenomegaly = Hemolytic crisis. (Low HB, jaundice, hepatosplenomegaly
77. A boy presents with complain of bleeding after tooth extraction, her mother give history that her paternal side male uncle have same issue of bleeding, due to which factor abnormality = Factor 8.
78. A girl has repeated admission for joint pain and abdomen pain her mother is Baloch, has beta thalassemia trait her father is sindhi. Hb 9, MCV 70 MCHC decreased diagnosis is = Sickle thalassemia syndrome.
79. N2O prolong exposure, human have increased risk of = Megaloblastic anemia.
80. Patients presented with lethargy generalized weakness, easy bruisability, fever, Hb 7 gm/dl platelets 50k , TLC 3000 and retic count 0.1 is most likely suffering from = Aplastic anemia (pancytopenia with low retic count)
81. In leukemia, eye involvement in which percentages = 80%
82. Prothrombin time is useful in which of these = Jaundice (PT is marker of hepatocyte functional integrity).
83. Which blood group is transfused successfully without reaction and can be used = O Negative to A negative.
84. How to differentiate cells in myelocytic stage = Staining of granules.
85. Patient present with fatigue, pallor and generalized body weakness and diagnosed as iron deficiency anemia, blood picture will show = Low MCV, low MCH low MCHC.
86. In thalassemia what's true = Increase iron.
87. Iron deficiency anemia, glossitis, cheilosis are the features of = Plummer Vinson syndrome.
88. A patient was operated for splenectomy peripheral blood smear of this patient shows = Howel Jolley bodies.
89. A patient presented with low grade fever night sweat and enlarge cervical lymph node lacunar cells with few reeds Sternberg cells seen which type it is = Nodular sclerosing type HL.
90. Which one of the following is responsible for blood clot retraction = Platelets.
91. Polycythemia Vera different from other types of Polycythemia in = Erythropoietin abnormality (low EPO).
92. Cells least abundant in circulating blood = Pluripotent stem cells > Basophils
93. A mother with blood group A+ gave birth to a baby with blood group O- . his father is O- . what will be chance of hemolytic reaction in newborn = Newborn will not develop Erythroblastosis fetalis.
94. Which factor helps in initiation of both intrinsic and extrinsic coagulation pathway = CA++ factor 4.
95. Hall mark of vitamin B12 deficiency is = Hypersegmented neutrophil.
96. A boy presented with bleeding gums, epistaxis and petechiae, test to be done for diagnosis = Bone marrow biopsy.
97. The deficiency of Christmas factor causes = Increase APTT (Hemophilia B).
98. Child having bleeding after circumcision and raised level of APTT. Diagnosis most likely is = Hemophilia A.
99. Small amount of blood loss for longer period of time = Microcytic Hypochromic (chronic blood loss)
100. A patient with low HB macrocytic RBC and Hypersegmented neutrophil with raised MCV likely diagnose is = Megaloblastic anemia
101. Natural anti thrombotic = Heparin.
102. Thrombin converting fibrinogen to fibrin release = Fibrinopeptide A.
103. Child presented with epistaxis and bleeding and having history of vaccination 1 week back = ITP.
104. Patient has anemia and Hypersegmented neutrophils are present on peripheral blood examination he is also having difficulty in balance which type of anemia he is suffering from = B12 Deficiency
105. A young girl with history of gum bleed and menorrhagia. Her peripheral blood smear shows large platelets and platelet count is 120000/L. What is the diagnosis = Bernard Soulier syndrome.
106. Hb 4 mg/dL with indirect jaundice, and reticulocytes 10 most likely = Hemolytic anemia.
107. Percentage of O+ blood group is = 47%.
108. Most common cause of pernicious anemia = Autoimmune atrophic gastritis.
109. Hair on end appearance on X – Ray what is the next appropriate test for diagnosis= HB electrophoresis.
110. What is the most appropriate treatment of VWD = Cryoprecipitate.
111. Which of the following has autosomal dominant inheritance = Hereditary spherocytosis.
112. After bleeding by a cut, the first homeostatic response to control the bleeding = Vasoconstriction.
113. Young girl with malaise and weight loss for 6 months, blast cells present with splenomegaly = ALL.
114. DIC is common presentation of = AML (M3).
115. What will be given in factor 9 deficiencies = FFP.
116. Patient having pallor fatigue raised mcv hyper segmented neutrophils, most common cause = Folate deficiency.
117. Auer rode are positive in = AML.

118. Pregnant lady come to clinic, her HB = 12 but after 2 mon, Hb level is 10. what is the cause = Hemodilution.
119. Main point where both extrinsic and intrinsic pathway meet = Factor 10.
120. lady with koilonychia blood picture will show = Decrease MCV MCH (Fe def anemia)
121. 18 years old female with menorrhagia epistaxis and marked decreased platelets count with giant platelets = ITP.
122. True about monocyte = Develop from Same precursor with neutrophils.
123. A child complaints of bleeding after minor injury's his mother give history of profuse bleeding during the time of circumcision, which test gives you clue of this condition = APTT (initial test to take clue is APTT, NOT factor 8 assay)
124. RBC breakdown results in = Release of iron which can be reutilized.
125. During Intravascular coagulation, first activated factor = Factor 12.
126. 10 years old girl presented with swollen joints after history of trauma, clotting profile shows prolongation of BT and APTT she has most likely deficiency of = Factor 8 major components.
127. Shape of RBCs is maintained through = Spectrin.
128. In sickle cell anemia, RBCs are spherical shaped, it is due to defect in = Cytoskeleton.
129. Child is pricked by needle, cause of excessive bleeding = Hemophilia.
130. A soldier present with 2 months history of fever, easy fatigue ability O/E hepatosplenomegaly and lymphadenopathy present. Labs reveal anemia h/o of bitten by fly, Diagnosis = Leishmaniasis.
131. A pregnant lady come to you for antenatal check-up, low serum ferritin, which deficiency expected = Iron.
132. Repeated blood transfusion increases the risk of = Hemosiderosis.
133. Vitamin K affects which factors = Factor 2,7,9,10
134. A female taking analgesic for backache presented with gum bleeding. She has fever 101 mild jaundice and hepatosplenomegaly. Hb 8 TLC 6500 neutropenia thrombocytopenia. On smear immature cells. Diagnosis = Drug induced anemia.
135. Fisherman presents with gum swelling and Purpura. Likely cause = Vitamin C Deficiency.
136. Female hand cut with knife, doesn't heal properly since last two weeks, wound is clean but presented with fever, Hb 6, RBS 130mg/dl what's the probable cause = Anemia (low Hb)
137. Regarding platelets Count = increase after splenectomy.
138. A patient has tingling sensations in his peripheral body and lab investigation reveal raised MCV. What is the most probable pathology = Vitamin B12 deficiency.
139. No agglutinin is present in blood group = AB+.
140. Iron stored in form of = Ferritin.
141. A patient having Polycythemia with facial congestion. likely raised in this patient is = Increase Hematocrit.
142. What is the characteristic feature of disease G6PD deficiency = Self-limiting hemolysis.
143. Child with multiple transfusions, splenomegaly, hematocrit 20% likely suffering from = Thalassemia.
144. A 12 yr old boy presented with progressive pallor easy fatigueability and lethargy her peripheral blood film showed absolute lymphocytes with more than 85% lymphocytes the most likely diagnosis is = Acute lymphoblastic leukemia.
145. Characteristic diagnostic test for folate deficiency = RBC folate level.
146. Hypercellular bone marrow is seen in = Myelodysplastic syndrome (only suitable given option in exam)
147. Bone marrow tap of patient with ITP shows = Increase megakaryocytes in bone marrow.
148. 6 yr old child was presented with pallor hepatosplenomegaly, HB = 5, most likely he is suffering from = Thalassemia.
149. Which factor activates after external injury = Factor VII.
150. Most important test to differentiate iron deficiency anemia from beta thalassemia = HbA2 electrophoresis.
151. A patient has anemia and hyper segmented neutrophils are present on peripheral blood examination he is also having difficulty in balance which type of anemia he is suffering from = B12 Deficiency.
152. A 7 yrs. child with history of fatigue pallor and fever. Mother gave history of pica child will be deficient in = Iron.
153. Regarding hereditary spherocytosis = RBC membrane defect
154. Thalassemia % in Pakistan = 5%.
155. Ineffective erythropoiesis occurs in = Erythroblastosis fetalis (also thalassemia)
156. Christmas disease increase bleeding what will be raised = APTT
157. Sickle cell anemia has which haemoglobin = HbS.
158. Reed Sternberg cell seen in = Hodgkin lymphoma.
159. Characteristics of Hodgkin lymphoma = contagious spread.
160. VWF disease BT and APTT deranged Problem = Platelet aggregation.
161. Most common cause of b12 deficiency = Pernicious anemia.
162. Poor prognostic factor for burn patient is = DIC.
163. Rh negative mother delivered a baby at 34 weeks with anemia pallor. Baby died 6 hours after transfusion. Autopsy findings = Basal ganglia staining.

164.Regarding neutrophils correct statement is = More phagocytic in blood stream.
165.Hb 6 mg/dl with indirect jaundice and reticulocytosis, most likely = Hemolytic anemia.
166.Warfarin mechanism of action = Competitively inhibits the vitamin k epoxide reductase complex 1 (VKORCI)
167.Diagnostic criteria of aplastic anemia = Fatty bone marrow.
168.Immediate reversal of Warfarin toxicity = FFPs.
169.A very young age patient presented with fever & his WBC were increased 60 folds is most likely suffering from = ALL.
170.Blood group antigens are.= Present on Hb surface.
171.A patient lady presented with low MCV low MCHC normal iron study profile which of the following need to be done in order to diagnose the case = HbA2.
172.A new borne after few hours of birth presented with active bleeding which of the following could be the possible management = Vitamin k administration.
173.A boy after circumcision has history of profuse bleeding which of the following factor will confirm the diagnosis = Factor 8 (Major) – to confirm , to take clue do APTT test.
174.A 22 yrs. pregnant lady who is Rh negative gives birth to Rh negative baby she has history of allergic reaction transfusion but she was transfused with Rh Positive blood accidentally. Which of the following is true = Anti D antibodies must be given immediately to lady.
175.A patient having ecchymosis & reduced Platelet count is suffering from = ITP.
176.Which of the following most common bleeding disorder from female carrier to male born = Hemophilia.
177.A person living at a altitude is most likely to have = Increase hemoglobin.
178.Child presents with action bleed from umbilical stump which of the following vitamin deficiency = Vitamin K.
179.Blood stem cells maturation is stimulated by = Growth factors.
180.Platelet adhesion to endothelium is caused by = Rough endothelial surface.
181.Rh blood group antigen present on.= Present on hemoglobin.
182.Bradynkinin involves of the following system = Kallikrein system.
183.Aplastic anemia diagnosis is done by which of the following = Trephine Bone marrow biopsy,
184.Which of the following is the largest cell in the blood = monocyte.
185.A boy with tender knee & bleeding history which of the following test will confirm the diagnosis = Factor 8 Assays.
186.A patient with IDA which of the following will confirm the diagnosis = Serum Ferritin
187.Anti H antibodies are present in which blood group = OH.
188.Pregnant lady in 1 st trimester having Hb of 11gm/dl on 3 rd trimester having Hb 9 gm/dl most likely due to = Physiological change.
189.Before starting oral anticoagulant warfarin therapy what test should be performed in order to analyse warfarin action = PT/INR.
190.Which of the following translocation is seen in AML = t (8:21).
191.B- lymphocytes produce = Plasma cells.
192.A 59 yrs old female with fatigue easy bruisability after small cuts and recurrent infection alongside fever from 2 week, show blast cells and auer bodies in smear. What is the likely diagnosis = Acute myeloid leukemia.
193.A 70 yrs old lady admitted into a hospital for long time is at high risk of developing = DVT.
194.A young patient with Hb level 5 g/dl WBC: 900 cells /mm ³ . Raised platelets and bilirubin. On blood smear there was polychromasia and raised relics. Diagnostic investigation will be = Coomb's test.
195.What is the first step in hemostasis after a vascular injury = Vascular Vasoconstriction.
196.A 48 yrs old woman presents with fever from 3 days. She also complains about urinary frequency beside loin (flank) pain. The white blood cells count is 40000/cmm. What is the next best step = Urine and blood culture.
197.A young patient underwent surgery of metallic valve replacement. He was sent home on regular drugs but he presented with nose blood (epistaxis) just 2 hours late. His platelets and Hb count are low and Pt is prolonged. What is the cause = Drug- induced.
198.A patient presents to clinic with his Hb level being 4 g/dl and coomb's test positive. What is the cause = Autoimmune hemolytic anemia.
199.A young patient with Hb level : 4.5 g/dl WBC: 700 cells /cmm. Raised smear there was polychromasia and raised relies. Diagnostic investigation will be = Coomb's test
200.In ITP which derangement is most common = Bleeding time.
201.8 th month pregnant lady with chronic ITP having ecchymosis and epistaxis. Her platelets count 4x10 and on full steroid dose what will be next suitable step = IV immunoglobulin.
202.7yrs old child episodes of epistaxis and gum bleed plt count normal. BT 16 MIN. APTT 32 sec. Diagnosis = VWD.
203.Immediate reversal of warfarin toxicity is done via = FFP.
204.A patient feels sensation of numbness in his extremities. His labs reveal Hb level 8g.dl MCV 110fl, platelet count 50x10 ⁹ /L and TLC 3.4x10 ³ /L. What is the diagnosis = Megaloblastic anemia.
205.A patient presents with tingling sensation and spastic contraction he is a case of = Tetany.

206. Which of the following is elevated in nasal polyps = Eosinophil.
207. Arterial blood as compared to venous blood has = increase PO ₂ .
208. A female presented with menorrhagia and her platelet count is 30000 mcl, which antibody test should be done = Antiplatelet antibody.
209. Which of the following proteins maintain the biconcave shape of the RBCs = Spectrin.
210. 9 month- old girl vaccinated two weeks back now develops rash over body and fever. Her CBC report reveals Hb 13g/dl Wbc 6x10 ⁹ /microliter and platelet count was low. Her peripheral smear showed large platelets. The condition is = ITP.
211. In uremic nephropathy there is = Normochromic normocytic anemia.
212. Which laboratory test would be suitable for vitamin K related factors = PT.
213. The type of anemia that occurs after gastrectomy is termed is = Pernicious anemia.
214. The nature of agglutinins is = Glycoprotein.
215. Which of the following is always present in anemia = Low Hemoglobin.
216. Increase PCO ₂ in venous blood will lead to = Increase volume of RBC.
217. In Rh blood group, Rh agglutinins = Develop in Rh negative woman pregnant with Rh positive fetus.
218. Hemoglobin synthesis begins at which stage = Early normoblast.
219. Vitamin – K dependent factor = Prothrombin
220. A patient with HB 8 platelet count 450000 with hyper cellular bone marrow diagnosis is = Iron def anemia.
221. A young female presented with fever, petechiae and epistaxis, best test to diagnose is = Bone marrow biopsy.
222. Which neoplasms develop from viral oncogenesis. = T- cell carcinoma (HTLV)
223. 45% hematocrit means = 45% of formed elements are RBC.
224. Burkitt lymphoma translocation = 8:14 (C-Myc translocation)
225. 8yrs old girl presented with iron deficiency anemia. Her spleen is palpable and frontal bossing is also present. What is the cause of her illness = Thalassemia Major.
226. An old patient presented to the emergency room for a fatigue dyspnea and chest pain which started Yesterday morning. He has been experiencing cough with sputum form many yrs. WBC 1000 hematocrit 25.4 % haemoglobin 8.4 d/L, MCV85 fl platelets 154000 and glucose 124 mg/dl. The clinical scenario is most consistent with which type of anemia = Anemia of chronic disease.
227. A 60 yrs old man w/ fatigue weakness and exercise intolerance. Labs: hemoglobin 9.1 mg/dl ferritin 9 ng mean corpuscular volume (MCV) 110 fl. Diagnosis = Megaloblastic anemia.
228. A patient with massive spleen. Spleen was palpable below 10 th ICS = Myelofibrosis.
229. Which of the following is consequence of Polycythemia Vera = Myelodysplastic syndrome.
230. A child with Erythroblastosis fetalis having blood group A+ve need blood transfusing which blood to give = A negative.
231. Warfarin affects which of following pathway of coagulation = Extrinsic.
232. A patient with Hb 6 TLC 3, PLT 60K. Spleen enlarged 4cm. To confirm cause of hypersplenism = Bone marrow biopsy.
233. The chance of bleeding in a patient with epidural will be greatest in = LMWH.
234. An anemia lady with reticulocyte 7%, jaundice, smear shows spherocytes. Test to be done = RBC survival study.
235. As compared to the arterial blood the venous blood has more = Packed cell volume (PCV)
236. regarding blood group antigens = secreted in saliva.
237. Monocyte macrophages derived from = Bone marrow.
238. Normal amount of iron in adult female = 2 gram.
239. Regarding lymphocytes= Inc. In viral infection.
240. Pulse oximeters = can't differentiate Methemoglobin from oxyhemoglobin.
241. Child having history of consumption of fast foods presented with anemia & raised MCV > 110 the most probable cause is = Folic acid deficiency (fast foods)
242. Vitamin k directly influences the reaction = Prothrombin to thrombin.
243. Continuous transfusion for thalassemia side effect = Hemochromatosis.
244. Side effects of Dicumarol = Delayed clotting, side effect of Dimercaprol = inc BT
245. 06 months old baby was vaccinated, now presents with rash all over body fever and CBC report showing Hb 14g/dl wbc 8x10 and decreased platelets peripheral smear shows large platelets. What is the diagnosis = ITP.
246. female gives birth at 35 th weeks, baby is slightly hydropic, peripheral blood smear shows nucleated RBCs and some erythrocytes marked Anisocytosis, Elliptocytosis what's is diagnose = Alpha thalassemia. (Hydrops fetalis)
247. Lady had a difficult labour at home in village. She was brought to hospital with history of PV bleed & oozing from gums for the last 04hours. Her CBC shows Hb = 6 g/dl platelets 20K, TLC 24000 with neutrophilia the peripheral blood film shows burr cells. Her Pt & APTT were prolonged. Most likely cause = DIC.
248. Patient presented with painful leg ulcer and having Howell jolly bodies on smear likely diagnose = Sickle cell anemia
249. Which of the following decrease in pregnancy = protein S (sometimes AT – III)

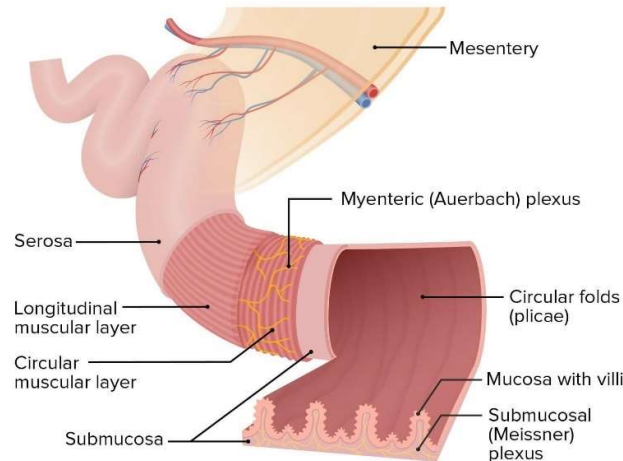
250. Female patient with Rheumatic fever taking methotrexate develop megaloblastic anemia due to = Folate deficiency.
251. Largest cell in blood is which of among following = monocyte (Overall largest cell is Megakaryocyte).
252. A male presented with fever rash on elbow and generalized cervical lymphadenopathy with TLC of 7230 what is suitable diagnosis = Infection mononucleosis.
253. Girl comes with increased fatigability with increased pigmentation on all body and splenomegaly having Hb 7, MCV 70 MCHC 35 and ferritin 3000. What is suitable management = Deferoxamine (iron overload)
254. A child has history of pica now having pallor fatigue and low Hb what is suitable diagnosis = Iron deficiency anemia.
255. Triad of sinus bradycardia absolute neutropenia Hepatosplenomegaly diagnose is = Typhoid.
256. After bacterial infection which cells will be seen = Neutrophilic leucocytosis.
257. An elderly lady taking rheumatoid arthritis drugs presents with weakness and malaise. Her retic count RBC WBC and platelets are low. Bone marrow is hypercellular. Likely cause is = megaloblastic anemia.
258. Regarding O- blood group = Has No antigen.
259. 40 yrs old man with backache apple green birefringence & Congo stain positive on damage to kidney with monoclonal antibody present he is most likely suffering from = Multiple myeloma.
260. A lady from a village has developed gum bleeding after delivery, raised Pt, APTT and low platelets neutrophil 2700 burr and cells are seen in peripheral smear and FDP raised diagnosis is likely = DIC.
261. A 2 yrs old present to you he was operated for acute abdomen and found intestinal obstruction. His small gut surgery done he is now presented to you with anemia and angular glossitis = Iron deficiency anemia (duodenal absorption)
262. Hodgkin lymphoma with missed cellularity association with which virus = EBV.
263. A 9yrs old male presented with epistaxis, BT > 20 minutes and increased APTT most suitable diagnose is = VWD.
264. Failure of bleeding clot retraction is due = Platelets dysfunction.
265. Pregnant lady with complain of DVT at 8 weeks which drug can be given = IV heparin.
266. Prostacyclin is produced by = Vascular endothelium.
267. Patient has H/o of recurrent bleeding and hemolytic anemia most likely pathology is = Ascorbic acid deficiency.
268. Iron hemostasis maintained by = Hepcidin.
269. A patient blood is agglutinates with anti sera A and D and contain agglutinin B, the blood group of the patient is = A+
270. 4 yrs old child with fever for 2 weeks, epistaxis, Hb = 5, TLC 100, platelets = 10. This is mostly likely = ALL.
271. Cause of petechial hemorrhages < 2mm is = Thrombocytopenia.
272. In uraemia what will increase = PT. (Functional PLT defect occurs in uremia)
273. A 45- yrs old man come to the emergency department after a motor vehicle accident resulting in a liver hematoma. On the third hospital day, he becomes suddenly short of breath. His chest x-ray is normal and he is diagnosed with a pulmonary embolus. What is the next best step in management = Heparin.
274. Patient of megaloblastic anemia, doctor advised Inj vitamin B12 IM Twice in a week due to deficiency of = Cobalamin.
275. After 4 yrs of Gastrectomy patient came with anemia which type of anemia he may have = Megaloblastic anemia
276. Aspirin decreases fever by decrease in which of following = Prostaglandins.
277. Patient started warfarin have petechiae and ecchymosis due to deficiency of = Protein C deficiency.
278. Low dose aspirin inhibit = Thromboxane A2.
279. Most common inherited thrombotic disorder Factor V Leiden > factor 12 deficiency.
280. To assess prolonged liver disease patient which test is performed = Albumin.
281. To check anti thrombin effect of heparin which test is used = APTT.
282. Finger injury which activates kinin and also coagulation by which factor = Hageman factor.
283. Platelet aggregation mediated by = Thromboxane A2
284. Low molecular weight heparin inhibit = Factor 10.
285. A blood group has which = Anti B Antibodies.
286. Most imp feature of platelets = Plug formation.
287. Which one controls iron homeostasis = Transferrin.
288. Exchange transfusion to A + baby with Erythroblastosis fetalis is done by = A -ve
289. A lady having jaundice + gall stone which of the following investigation will confirm the diagnosis = ALP.
290. Microcytic hypochromic anemia ferritin and TIBC normal confirmatory investigation will be = HbA2.
291. In intrinsic damage which factor cause activation of coagulation = Factor 12 (Hageman factor).
292. Hereditary spherocytosis defective protein is = Ankyrin > Spectrin.

GASTROINTESTINAL SYSTEM (GIT)**STRUCTURE / WALL OF GIT**

Mucosa (Innermost layer)	<ul style="list-style-type: none"> Mucosa has three parts: Epithelium, lamina propria and muscularis mucosa. <ul style="list-style-type: none"> Epithelium: may be stratified squamous or columnar depending upon part of Gut Lamina propria: beneath epithelium, has macrophages, lymphocytes, fibroblasts. Muscularis mucosa: thin layer of smooth muscles from esophagus to anus Erosions are related to mucosa only
Submucosa	<ul style="list-style-type: none"> It has blood vessels and submucosal Meissner's plexus – controls secretions. Abundant glands are present in submucosa of GIT (oral cavity) Location of esophageal varices is also submucosa
Muscularis externa	<p>Muscular layer consists of 2 layers: inner circular and outer longitudinal smooth muscle layer, except for -- stomach and esophagus.</p> <ul style="list-style-type: none"> Inner circular layer contraction causes decrease in diameter of gut lumen. Outer longitudinal layer contraction causes shortening of the gut segment. Muscular layer has myenteric (Auerbach) nerve plexus – controls gut motility. ❖ Esophagus → Skeletal + Smooth muscles ❖ Stomach → Three layers – inner oblique, middle circular, outer longitudinal smooth muscle layer. An extra layer for grinding and mixing of food. ❖ Rest of whole GIT (intestines) – inner circular + outer longitudinal layer ❖ Ulcers can extend into submucosa, inner or outer muscular layer
Serosa	<ul style="list-style-type: none"> Serosa is the Outermost layer of intraperitoneal organs e.g., stomach. Adventitia is present in retroperitoneal organs or part of organs.

INNERVATION OF GIT

Extrinsic supply	<u>Autonomic nervous system</u> <ol style="list-style-type: none"> Parasympathetic system -- excitatory for functions of GIT by Vagus and pelvic nerves <ul style="list-style-type: none"> Vagus nerve supplies esophagus, stomach, pancreas, and upper large intestine Pelvic nerve innervates lower large intestine, rectum, and anus. Sympathetic system-inhibitory for gut functions via T8-L2 fibers
Intrinsic supply	<u>Enteric Nervous system:</u> <ul style="list-style-type: none"> Uses local reflexes to relay information within GIT, also called second brain. Controls most of GIT functions including secretions and motility even in the absence of Extrinsic innervation. It consists of 2 nerve plexuses as given below: <ol style="list-style-type: none"> Meissner (submucosal) plexus – controls secretions and blood flow by receiving sensory information from chemoreceptors and mechanoreceptors in GIT. Auerbach (Myenteric) plexus – controls motility of GI tract smooth muscles



REGULATORY SUBSTANCES IN GIT

They include 4 official hormones (and candidate hormones), 2 paracrine and various Neurocrines.

Official hormones

Gastrin	<ul style="list-style-type: none"> Secreted by G cells (stomach antrum, duodenum) in response to meal (small peptides & Amino acids), gastric distension, vagus (via GRP) Biological activity resides in four C-terminal amino acids. It inc gastric H⁺ secretion, growth of gastric mucosa, \uparrow gastric motility Gastrin is Inhibited by acidity (H⁺, PH < 1.5) and somatostatin. Phenylalanine and tryptophan -most potent stimulator for gastrin release Gastrin increases by chronic PPIs use, chronic atrophic gastritis (e.g., H pylori) and \uparrow \uparrow by Zollinger-Ellison syndrome (Gastrinoma)
CCK	<ul style="list-style-type: none"> Secreted by I cells (duodenum, jejunum) in response to fatty meal (fatty acids, monoglycerides) and small peptides or amino acids Has 33 amino acids- structural homology with gastrin (five C- terminal AA) Actions include inc gallbladder contraction, relaxation of sphincter of Oddi, inc pancreatic secretions (enzymes rich) and growth of exocrine pancreas. CCK delays gastric emptying but increases intestinal motility. Triglycerides (TAGs) don't stimulate CCK release- can't cross gut membrane
Secretin	<ul style="list-style-type: none"> Secreted by S cells (duodenum) in response to gastric acid (H⁺) and fatty acids when they reach the lumen of duodenum. It is the first hormone that was discovered. Actions: inhibits gastric H⁺ release, stimulates pancreatic HCO₃ secretion (neutralizes gastric acid in duodenum) and growth of pancreatic mucosa Secretin inc Bile production by stimulation of HCO₃ & H₂O by liver It inhibits motility of both stomach and intestines and inc insulin secretion
GIP	<ul style="list-style-type: none"> GIP = Glucose-dependent insulinotropic peptide/gastric inhibitory peptide Secreted by K cells (duodenum, jejunum) in response to fatty acids, amino acids, and Oral glucose. It is homologous to secretin and glucagon. The only GIT hormone released in response to fats, protein, and carbs. GIP inc insulin secretion and dec H⁺ secretion Oral glucose load inc insulin secretion more due to GIP secretion

Candidate hormones

Motilin	<ul style="list-style-type: none"> Secreted in fasting by small intestine- increases GI motility. Produces migrating motor complexes/inter-digestive myoelectric complexes. Erythromycin (Motilin receptor agonist) inc intestinal motility
GLP-1	<ul style="list-style-type: none"> Binds to β cells in pancreas to stimulate insulin secretion. GLP-1 analogues e.g., Exenatide are helpful in treating type 2 diabetes.
Leptin	<ul style="list-style-type: none"> Secreted by Fat (adipose) cells. Decreases appetite (dec weight) by stimulating anorexigenic neurons
Ghrelin	<ul style="list-style-type: none"> Increases appetite (weight gain) G for giant and gain of weight/Ghrelin. Released by stomach in fasting and decreased by food intake Ghrelin inc in Prader-Willi syndrome, dec after gastric bypass surgery
PP	<ul style="list-style-type: none"> Pancreatic polypeptide secreted by pancreas (F cells). inhibits secretions of pancreas.

Paracrines

Histamine	<ul style="list-style-type: none"> Secreted by mast cells of gastric mucosa and stimulates gastric acid (H⁺) secretion directly by potentiating effects of gastrin and vagal stimulation. Keep in mind, gastrin inc the acid (H⁺) secretion mainly by entero-chromaffin like cells (ECL) leading to histamine release, rather than direct action
Somatostatin	<ul style="list-style-type: none"> Secreted by D cells (pancreas, GI mucosa) in response to gastric acid (H⁺) inhibits acid secretion and \downarrow secretion of all GIT hormones (stasis/stops) \downarrow gastric, pancreatic and small gut secretions, also dec insulin, glucagon and inhibits gallbladder contractions Somatostatin inhibited by vagal stimulation. Octreotide is its analogue- useful in acromegaly, GI bleed, carcinoid syndrome

Neurocrines

VIP	<p>Secreted by parasympathetic ganglia in GIT sphincters, gallbladder, and small gut in response to distension and vagal stimulation and causes relaxation of intestinal smooth muscles and sphincters including lower esophageal sphincter. It increases intestinal water and electrolyte secretion and VIP inhibited by adrenergic input.</p> <p>It stimulates pancreatic HCO₃ secretion but inhibits gastric acid secretion.</p> <p>VIPoma (non-alpha, not β pancreatic tumor) causes diarrhea, \downarrow H⁺ and \downarrow K⁺.</p>
GRP	GRP/Bombesin stimulates gastrin release from G cells
Enkephalins	<p>Stimulates GI contraction especially lower esophageal, pyloric and ileocecal valve.</p> <p>Inhibits intestinal secretion of fluid and electrolytes- the basis for usefulness of opiates in diarrhea.</p>
Nitric oxide (NO)	<p>Released from stomach, inc smooth muscle relaxation including lower esophageal sphincter (LES), loss of NO is implicated in \uparrow LES tone of achalasia</p>

GIT MOTILITY

Contractile tissue of GIT is almost **unitary** smooth muscle except pharynx, upper 1/3rd esophagus, and external anal sphincter where it is striated (skeletal muscle)

Phasic contraction: rapid and transient, occurs in esophagus, antrum of stomach and small gut.

Tonic contraction: slow and sustained, occurs in sphincters, lower esophagus, ileocecal valve.

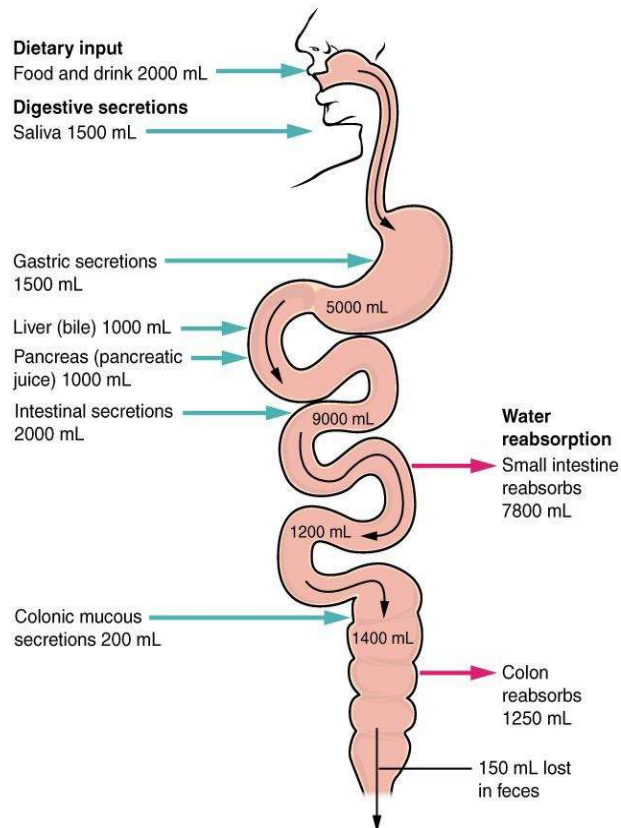
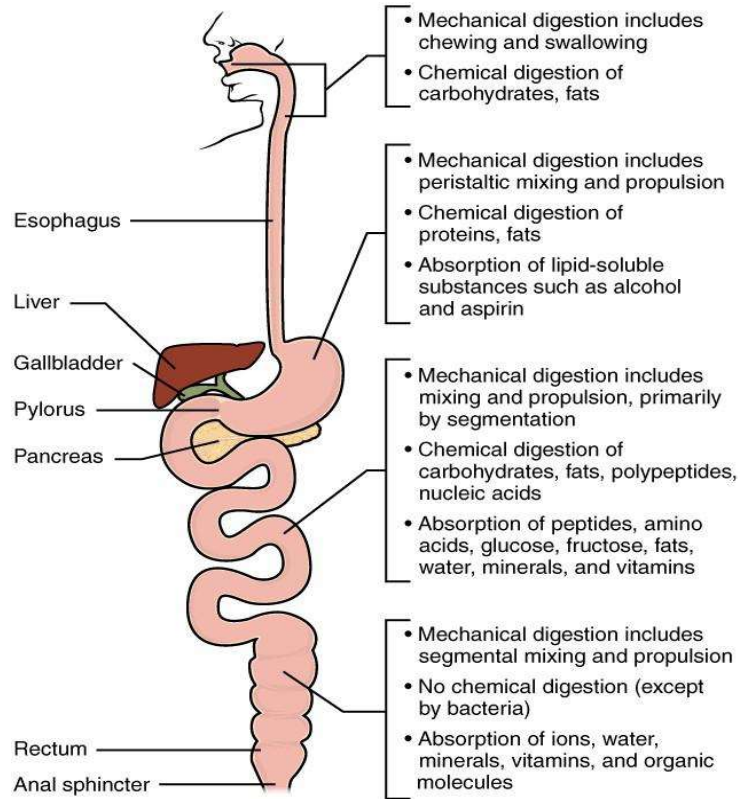
Recalling the muscular layer of GIT (inner circular and outer longitudinal smooth muscles layer)

- Contraction of **circular** muscle causes **decrease in diameter** of gut lumen.
- Contraction of longitudinal layer causes shortening of the gut segment.

Slow waves or (Basic electric rhythm)	<p>They are basic electric rhythm- not true action potentials but determine action potential. Slow waves originate from interstitial cells of Cajal (pacemakers) - occur spontaneously.</p> <p>Frequency: varies along GI tract, highest in duodenum and lowest in stomach. The sequence:</p> <p>➤ Duodenum (12 cycles/ min) > ileum > Stomach (3 cycles/min)</p> <p>Mechanism: Depolarization by opening of slow Ca⁺ channels and repolarization via opening of K⁺ channels. Interstitial cells of Cajal are pacemaker cells of GI tract</p>
Chewing Swallowing Peristalsis	<ul style="list-style-type: none"> ❖ Chewing lubricates food and decreases size of particles for the enzymes to act. ❖ Swallowing centre present in medulla- involves Glossopharyngeal & Vagus nerve. ❖ During swallowing: nasopharynx + glottis closed (vocal cords approximated especially false vocal cords), breathing stops (transient apnoea), propels food into esophagus. ❖ Upper esophagus sphincter relaxes that allows propelling of food via Primary peristalsis. ❖ primary peristalsis is assisted by gravity. Meanwhile, lower esophageal sphincter relaxes. and secondary peristaltic contractions clears the esophagus of any remaining food. ❖ lower esophageal relaxation is vagally mediated by VIP as neurotransmitter. ❖ proximal body of stomach + fundus = orad region, it relaxes i.e., receptive relaxation to allow food bolus to enter the stomach. 2ndry peristalsis is not gravity dependent.

Gastric motility	<p>Stomach consists of fundus, body and antrum</p> <ol style="list-style-type: none"> 1. Receptive relaxation: Distention of stomach initiates vagovagal reflex (participated by CCK) – Oral region (fundus + proximal body) relaxes to accommodate food 2. Mixing and digestion: 3-5 slow waves/min in the caudad region (antrum + distal body) set the maximal frequency of contraction to mix + propel the food into duodenum During fasting, contractions (migrating motor complexes mediated by Motilin) occur every 90 min intervals to clear the residual food from stomach. 3. Gastric emptying: factors affecting Gastric motility are as follows: <ul style="list-style-type: none"> ○ Mixing waves and weak peristaltic waves pass the food in duodenum (now called Chyme) ○ Fundus removal causes dec gastric compliance > dec receptive relaxation ○ Antrum removal decreases acid production (loss of G cells – Gastrin) ○ Pylorus removal causes the solids to pass easily
Small intestine motility	<ol style="list-style-type: none"> 1. Segmentation contractions: back and forth movements causing mixing of food only 2. Peristaltic contractions: Propulsive movements by enteric nervous system cause contraction behind and relaxation in front of bolus, thus, pushing the chyme forward ❖ Serotonin initiates this peristaltic reflex here 3. Gastroileal reflex: mediated by ANS (via gastrin), food in stomach triggers inc peristalsis in ileum + relaxation of ileocecal sphincter, contents are delivered into large intestine
Large intestine motility	<ol style="list-style-type: none"> 1. Cecum and Proximal colon: segmentation contractions here mix the contents – responsible for Haustration, proximal colon distends while ileocolic sphincter contracts. Mass movements 1-3/day causes colonic contents to move distally for long distances. Maximum H₂O absorption occurs in proximal colon than other parts of large gut. 2. Distal colon: semi-solid fecal moves slowly into rectum 3. Rectum, anal canal, and defecation: rectum filled with fecal material contracts and internal anal sphincter relaxes – rectosphincteric reflex. When convenient to defecate, external anal sphincter relaxes voluntarily. 4. Gastrocolic reflex: presence of food in stomach inc the motility of colon and frequency of mass movements. It has two components: Stretching of stomach by food initiates rapid parasympathetic component Slow hormonal component is mediated vis CCK and gastrin. Defecation is initiated by mass movements and carried by sacral parasympathetic nerves (S₂, S₃, S₄), defecation reflex is Rectoanal in adults while gastrocolic in infants After eating food, if one feels the need to defecate – that is via Gastrocolic reflex
<u>VOMITING</u>	<ul style="list-style-type: none"> ○ Vomiting centre in medulla is stimulated by tickling the back of throat, gastric distension, and vestibular stimulation (motion sickness) ○ Chemoreceptor trigger zone in 4th ventricle is activated by emetics, radiation, and vestibular stimulation. ○ A wave of reverse peristalsis beginning in small gut eventually pushes GI contents into esophagus, if upper esophageal sphincter remains closes – retching occurs. ○ If pressure in the esophagus becomes high enough to open the upper esophageal sphincter – vomiting occurs

	GIT motility / Emptying	Intestinal motility
Stimulants	Vagal stimulation Gastrin, Motilin, GRP, Histamine, macrolides	parasympathetic system Cck, gastrin, motilin, serotonin
Inhibitors	Adrenergic (sympathetic) stimulation Fat (via CCK), CCK, secretin, GIP, acidity (acid - H ⁺) in duodenum and distension of duodenum	Sympathetic stimulation Secretin Glucagon



GIT SECRETIONS																	
Salivary secretions	<ul style="list-style-type: none"> Saliva has; high volume, hypotonic, low Na⁺ & Cl⁻ but high K⁺ and HCO₃⁻, amylase, lingual lipase. Initial starch digestion by alpha amylase, while initial triglyceride digestion by lingual lipase Composition of saliva varies with salivary flow rate; 1. At highest flow rates, its composition is similar to plasma i.e low K⁺ and highest Na⁺ & Cl⁻, just like its initial secretion from acinus. 2. At lowest flow rates, it has highest K⁺ but lowest osmolarity (due to low Na⁺ Cl⁻ and HCO₃⁻) 3. Thick saliva is produced by sympathetic activation via alpha 1 and beta 1 receptors. Salivary secretion is increased by parasympathetic and sympathetic system. Acetylcholine > VIP > substance P increase salivary secretions. VIP induces splanchnic vasodilation and increases salivary flow. Saliva production is inhibited by atropine, sleep, and dehydration 																
Gastric secretions	<table border="1"> <thead> <tr> <th></th><th>Stimulated by</th><th>Inhibited by</th></tr> </thead> <tbody> <tr> <td>HCL</td><td>Gastrin, parasympathetic system, histamine</td><td>Low stomach pH, Chyme in duodenum, atropine, PPIs, somatostatin, cimetidine</td></tr> <tr> <td>Pepsinogen</td><td>Parasympathetic system</td><td></td></tr> <tr> <td>Intrinsic factor</td><td colspan="2">Secreted by parietal cells in the fundus of stomach. IF helps in Vit B12 absorption</td></tr> <tr> <td>Gastrin</td><td>Secreted by G cells in antrum of stomach. Stimulated by vagal stimulation, peptides</td><td>Somatostatin acid in the stomach</td></tr> </tbody> </table> <ul style="list-style-type: none"> Parietal cells in fundus (body) of stomach secrete → HCL + intrinsic factor. Chief cells (fundus/body) produce pepsinogen. G cells (in antrum) produce gastrin Mucous cells in antrum produce mucus and pepsinogen 			Stimulated by	Inhibited by	HCL	Gastrin, parasympathetic system, histamine	Low stomach pH, Chyme in duodenum, atropine, PPIs, somatostatin, cimetidine	Pepsinogen	Parasympathetic system		Intrinsic factor	Secreted by parietal cells in the fundus of stomach. IF helps in Vit B12 absorption		Gastrin	Secreted by G cells in antrum of stomach. Stimulated by vagal stimulation, peptides	Somatostatin acid in the stomach
	Stimulated by	Inhibited by															
HCL	Gastrin, parasympathetic system, histamine	Low stomach pH, Chyme in duodenum, atropine, PPIs, somatostatin, cimetidine															
Pepsinogen	Parasympathetic system																
Intrinsic factor	Secreted by parietal cells in the fundus of stomach. IF helps in Vit B12 absorption																
Gastrin	Secreted by G cells in antrum of stomach. Stimulated by vagal stimulation, peptides	Somatostatin acid in the stomach															
Pancreatic secretions	<ul style="list-style-type: none"> Pancreatic juice is high volume and isotonic (same Na & Cl conc. as plasma) It has higher HCO₃⁻ than plasma but much lower Cl⁻ than plasma Regardless of the flow rate, composition of pancreatic secretions is isotonic. At higher flow rate, composition is isotonic to plasma (high HCO₃⁻ and Na⁺) At lower flow rates, composition is isotonic- having high Cl⁻ and HCO₃⁻) Pancreas secretes alpha amylase (starch digestion) lipase (fat digestion) and proteases. Pancreatic lipase- specific marker for acute pancreatitis Proteases include trypsin, chymotrypsin, elastase, and carboxypeptidases. They are secreted as proenzymes (inactive form) called zymogens. Trypsinogen is converted to active enzyme trypsin by Enterokinase secreted from brush border of duodenum & jejunum. Trypsin → activation of other proenzymes and cleaving of trypsinogen additional molecules into active trypsin (+Ve feedback) i.e trypsin mediated trypsin release. Pancreatic secretions are increased by secretin, CCK and Ach Secretin increases pancreatic Bicarbonate rich secretions. CCK increases enzyme rich secretions of pancreas. 																
BILE	<ul style="list-style-type: none"> Composed of bile salts, phospholipids, cholesterol, bilirubin, and water. Bile salts are conjugated to glycine or taurine, making them water soluble. Bile is synthesized in liver hepatocytes and concentrated + stored in gallbladder. CCK released in response to small peptides and fatty acids in duodenum, conveys gallbladder that bile is needed to emulsify and absorb lipids in duodenum, causes contraction of gallbladder + relaxation of sphincter of Oddi to release bile. Bile salts are absorbed in terminal ileum where Na-bile co-transporter is present which helps in recirculation it to liver (enterohepatic circulation) and excreted in feces 																

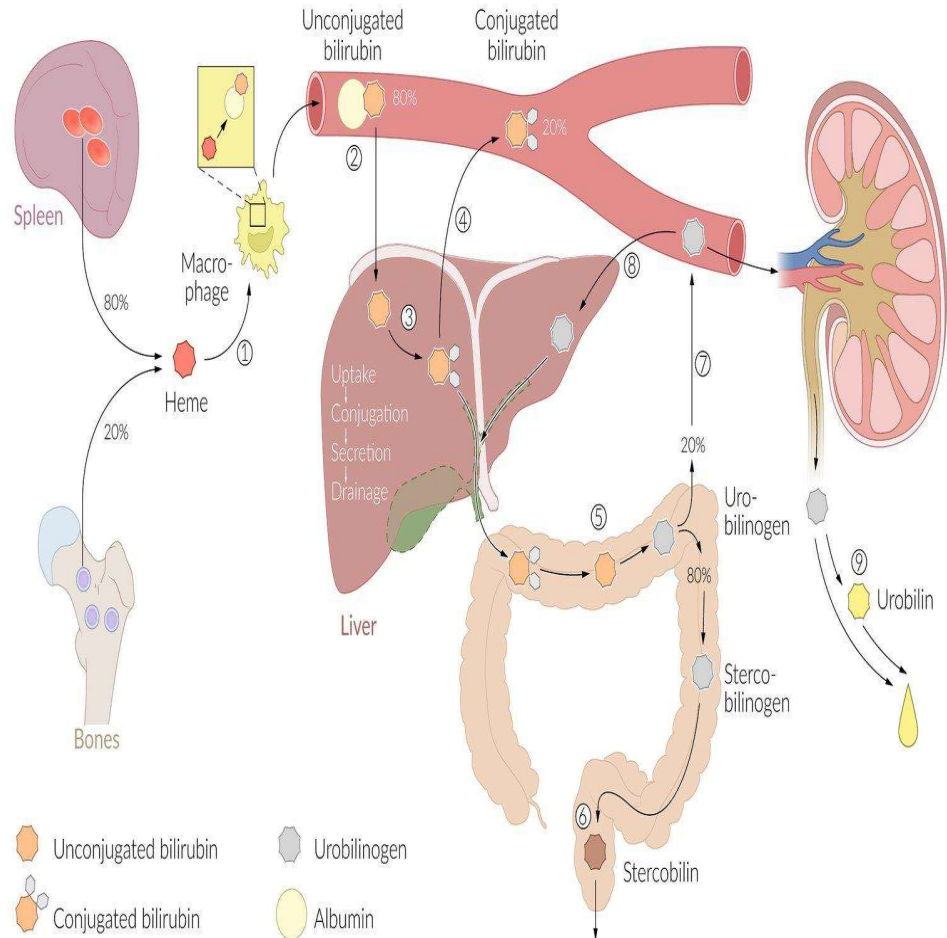
Functions:

Bile salts aid in digestion and absorption of lipids and fat-soluble vitamins by emulsifying and solubilizing them in **micelles**.

Bilirubin and cholesterol excretion (body's primary mean for elimination and antimicrobial activity)

Micelles: formed by bile acids, contain free fatty acids, monoglycerides and aid in fat absorption

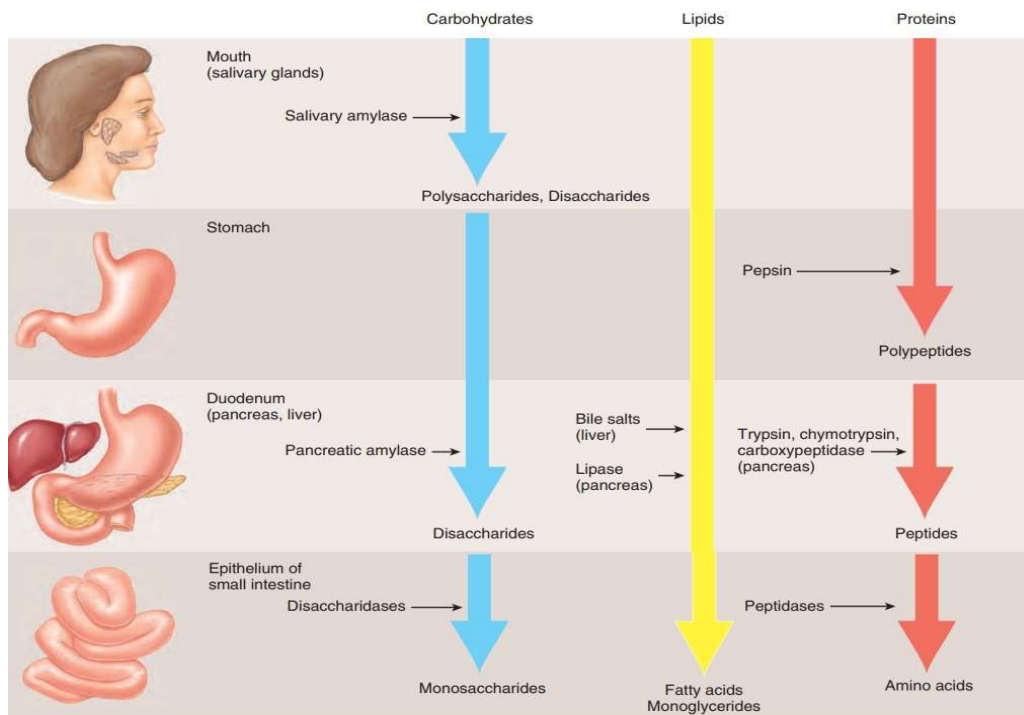
- Decreased absorption of bile salts at distal ileum e.g in ileal resection/chron's disease leads to impaired enterohepatic circulation resulting in Steatorrhea or bile acid diarrhea with increased incidence of Calcium oxalate renal stones



DIGESTION AND ABSORPTION OF NUTRIENTS

Small intestine is the main site for digestion and absorption of Carbohydrates, lipids, and proteins, while the surface area for absorption is increased by brush border(microvilli) of enterocytes.

Carbohydrates	<ul style="list-style-type: none"> ❖ Digestion of carbs starts in the mouth by salivary amylase. ❖ Must be digested to monosaccharides (glucose, galactose, fructose) for absorption to occur. ❖ All are transported to blood by GLUT 2 (Liver, pancreas B cells) ❖ Fructose is taken up by GLUT 5 via facilitated diffusion. ❖ Glucose and galactose are taken up by Na⁺ dependent co-transport (SGLT-1) ❖ Lactose intolerance due to deficiency of brush border lactase results in osmotic diarrhea ❖ D-xylose test absorption test distinguishes GI mucosal damage from other causes of malabsorption
Proteins	<ul style="list-style-type: none"> ❖ Digestion mainly starts in the stomach by pepsin that breaks proteins into peptide bonds. ❖ Digestion is completed in small intestine by pancreatic enzymes trypsin, chymotrypsin, and carboxypeptidases. ❖ Absorption occurs in the form of free amino acids (Na⁺ dependent co-transport) while dipeptides and tripeptides via H⁺ dependent cotransport. ❖ Short chain fatty acids absorbed in colon while long chain FAs absorbed in jejunum.
Lipids	<ul style="list-style-type: none"> ❖ Lingual lipase in saliva, pancreatic lipase, and bile acids (emulsify) help in digestion.
H₂O & Electrolytes	<ul style="list-style-type: none"> ❖ Maximum water and electrolytes absorption occurs in jejunum – 80 % and 10 % in colon. ❖ 10 % water is excreted in feces. ❖ Maximum loss of H₂O (e.g diarrhea) occurs from colon. ❖ Passive H₂O and electrolytes absorption (Aldosterone independent) occurs in jejunum. ❖ Active (aldosterone dependent) water and salts absorption in colon. ❖ Ileum resection results in increased water content of feces > dec bile salts absorption. ❖ Colostomy results in secretory diarrhea. Jejunostomy or ileostomy → osmotic diarrhea. ❖ Jejunostomy + ileostomy combined → osmotic + secretory diarrhea.
iron	<ul style="list-style-type: none"> ❖ Absorbed as Fe²⁺ in duodenum. Free iron (e.g., in meat) binds apoferritin-transported in blood.
Calcium	<ul style="list-style-type: none"> ❖ Absorbed in duodenum, requires active form of Vit D (calcitriol/cholecalciferol) for absorption.
Folate (Vit B9)	<ul style="list-style-type: none"> ❖ Absorbed in jejunum. Only Vit B12 and folate absorption is Na⁺ dependent.
Vit B12	<ul style="list-style-type: none"> ❖ Absorbed in terminal ileum (requires intrinsic factor present in stomach). ❖ Transport of Vit B12 needs transcobalamin 2.
Fat soluble Vit	<ul style="list-style-type: none"> ❖ Absorbed in small gut with lipids (micelle formation).



DISEASES OF ORAL CAVITY & GI TRACT

ORAL CAVITY - SUMMARY

- Cleft lip and cleft palate is the most common congenital anomaly of oral cavity
- Incidence of tumors is high in Parotid gland, while, stones mostly affect submandibular gland
- Submandibular **sialolithiasis (stone)** is due to dehydration, trauma or infection, presents with pain-exaggerated while eating and swollen/tender submandibular region. It is managed with hydration, NSAIDs, sialagogues (e.g chewing gum), massaging/probing, antibiotics (dicloxacillin), lithotripsy or endoscopic removal.
- **Ranula** is a mucous retention cyst in the floor of mouth that presents with swelling (often blue colored) under tongue and managed with marsupialization, aspiration or incision and drainage
- **Sjogren syndrome** is an autoimmune disorder involving salivary glands, characterized by xerostomia (dry mouth), keratoconjunctivitis sicca (dry eyes) and increased incidence of lymphoma. It is associated with connective tissue disorders, mostly **Rheumatoid arthritis**
- In the Jaw of a diabetic patient, if granuloma with multiple abscesses and yellow discharge is found → suspect actinomyces Israeli (feature- sulfur granules containing organism)
- Pre-malignant lesion of oral cavity include leukoplakia (most common), Erythroplakia (most lethal), and chronic ulcer
- Most common pre-malignant condition of oral cavity is oral submucosal fibrosis (OSF) -betel nut is the most common risk factor associated with OSF. Therefore, incidence of OSF and oral cancer is high in Karachi.
- Mouth ulcer is also a pre-malignant lesion in adults leading to oral cancer.
- **Lichen planus** is the most lethal premalignant condition that is erythematous to violaceous flat-topped papules, often with white lacy lines (Wickham's striae) on the oral cavity, wrists or forearms and genitalia. Incidence of lichen planus for malignancy is 1-10% in 10-15 years.
- **Oral cancer** is mostly squamous cell carcinoma and in more than 50% cases involves tongue (lateral border most often site) associated with tobacco (smoking), alcohol, HPV, betel nut, chronic irritation from jagged teeth
- **Pleomorphic adenoma** is the most common salivary gland tumor that mostly involves parotid gland in 90% cases. It is a benign tumor of mixed variety (epithelial + mesenchymal component) that presents with painless mobile mass. Treated mostly with superficial parotidectomy (facial palsy is a feared complication as it is the most superficial in the gland). The tumor has tendency to recur after excision and may rarely (1 % cases) transform into malignancy
- **Warthin tumor** is a benign cystic tumor, 8% incidence, often bilateral, common in smokers and cystic fluid has motor oil quality. It is also known as papillary cystadenoma lymphomatosum.
- Most common malignant salivary gland tumor is **Mucoepidermoid carcinoma**. It is also painless and slow growing like pleomorphic adenoma and has mucinous + squamous component
- Salivary gland tumor having tendency for perineural invasion is Adenoid cystic carcinoma
- Common site for cancer of lip is Lower lip (best prognosis among all oral malignancies)
- Worst prognosis among oral malignancies is of carcinoma of floor of mouth
- Cancer of oral cavity containing rete ridges, pleomorphism, inc N/C ratio is Squamous cell CA > Verrucous carcinoma
- Ludwig angina is the cellulitis of floor of mouth that may be caused by anaerobes after a dental procedure.
- Oral ulcers respond well to nystatin (for adults) and miconazole (for child)
- Aphthous ulcer is the most common ulcerative condition of oral mucosa, presents as a painful punched-out sore on oral or genital mucous membranes. They are also called aphthae, aphthous stomatitis and canker sores. They are likely due to T cell mediated immune dysfunction
Recurrent aphthous stomatitis can also result from a nutritional deficiency, particularly lack of iron, vitamin B₃ (as in pellagra), vitamin C (as in scurvy), folic acid, or vitamin B₁₂. Treatment: steroids, doxycycline
- Bacher's disease: autoimmune, HLA B-51 involved, triad of oral aphthous ulcers, genital ulcers, and ocular disease (hypopyon). Also called silk road disease due to prevalence along that region. Managed by steroids & immunosuppressants

- Most common premalignant condition leading to squamous cell CA of **skin** is Bowen's disease.
- Premalignant condition on face (cheeks) that need to be excised is actinic keratosis

Most common	<ul style="list-style-type: none"> • Premalignant Condition = Submucosal Fibrosis • Premalignant Lesion = Leukoplakia • Oral carcinoma = squamous cell cancer (lateral border of tongue) • Benign salivary gland tumor = pleomorphic adenoma • Malignant salivary gland tumor = Mucoepidermoid carcinoma
Most lethal	<ul style="list-style-type: none"> • Premalignant Condition = Lichen Planus • Premalignant Lesion = Erythroplakia
Note the difference of word -- lesion and condition	

DISEASES OF THE ESOPHAGUS

Congenital (TEF)	<ul style="list-style-type: none"> • Most common congenital anomaly of esophagus is tracheoesophageal fistula (TEF) • Neonates: drool > choke > cyanose in TEF
Dysphagia	<ul style="list-style-type: none"> • Difficulty in swallowing; due to pharyngeal or esophageal (commonly) pathologies e.g stricture, infection, inflammation, motility disorder or neoplasm. • Odynophagia is the painful swallowing - commonly due to esophagitis • Progressive dysphagia: dysphagia to solids followed by liquids too and it indicates malignancy of esophagus (e.g squamous cell CA) > stomach • Dysphagia only to liquids may be associated with neuromuscular disorder or achalasia
Esophagitis	<ul style="list-style-type: none"> • Associated with reflux, infections (Candida in HIV, HSV-1, CMV), irritants (e.g caustic) ingestion or pills induced esophagitis e.g Bisphosphonates, tetracycline, Iron, NSAIDs, KCL • HSV-1 esophagitis – punched out ulcers, while, CMV esophagitis – Linear ulcers • Candida related esophagitis – white pseudomembrane • Eosinophilic esophagitis: eosinophils infiltration in the esophagus often in atopic patients due to multifactorial etiology. Food allergens cause dysphagia and food impaction • Esophageal rings and linear furrows seen on endoscopy → Eosinophilic esophagitis
Mallory Weiss tears	<ul style="list-style-type: none"> • Longitudinal mucosal/submucosa lacerations of Gastroesophageal junction (GEJ) due to prolonged retching or vomiting (alcoholics/bulimia nervosa). • Presents with painful hematemesis ± abdominal or back pain
Boerhaave's syndrome	<ul style="list-style-type: none"> • Transmural (full thickness) tear or esophageal rupture-seen commonly in alcoholics due to prolonged violent retching.
Esophageal perforation	<ul style="list-style-type: none"> • Most commonly iatrogenic following instrumentation, other causes; foreign body, trauma, neoplasm, or spontaneous rupture • May present with pneumomediastinum, subcutaneous emphysema (crepitus in neck or chest wall)
Gastroesophageal reflux disease (GERD)	<ul style="list-style-type: none"> • Incompetent lower esophageal sphincter leads to reflux of gastric contents into esophagus associated with smoking, alcohol, soft drinks/hot liquids, and spicy food. • Presents with heartburn, regurgitations, pharyngitis, oral soreness, bitter taste of mouth • Complications: stricture, esophagitis, ulceration, metaplasia (Barret esophagus) • 24 hour pH monitoring – gold standard or most accurate investigation • Endoscopy is the investigation of choice • Management: Avoid the triggering agents, take meal at night 4 hours before bedtime, reduce weight if obese, PPIs (omeprazole) are the drug of choice.
Barret Esophagus	<ul style="list-style-type: none"> • It is a complication of long standing GERD (10%) , a pre malignant condition in which squamous epithelium of esophagus is replaced by metaplastic columnar epithelium of intestinal type containing goblet cells. • Also associated with esophagitis, ulcers and inc risk of esophageal adenocarcinoma • Endoscopy is the investigation of choice • 4cm above GEJ involvement is required for diagnosis of Barret esophagus

	<p>Barret metaplasia without dysplasia: PPIs + endoscopy 3-5 yearly to exclude dysplasia or carcinoma</p> <p>Low grade dysplasia: PPI + 6 monthly endoscopic surveillance to exclude high grade dysplasia or carcinoma</p> <p>High grade dysplasia: PPIs + endoscopic resection/ablation is the modality of treatment</p>
Achalasia or achalasia cardia	<ul style="list-style-type: none"> Failure of lower esophageal sphincter (LES) to relax due to degeneration of inhibitory neurons (containing NO & VIP) in myenteric plexus of esophageal wall Primary achalasia is idiopathic, but secondary achalasia may be due to Chaga's disease or malignancies outside the esophagus causing mass effects Features: progressive dysphagia to solids and liquids (especially) in middle aged females, sometimes may have chest pain due to esophageal spasm. Barium swallow: dilated esophagus with area of distal stenosis i.e bird's beak appearance Esophageal manometry is the gold standard investigation → uncoordinated or absent peristalsis with raised LES tone or resting pressure Associated with risk of esophageal squamous carcinoma Treatment: surgery, Botox injection, Ca⁺ channel blockers and endoscopic procedures
Diffuse or distal esophageal spasm	<ul style="list-style-type: none"> Also known as nutcracker esophagus due to Corkscrew appearance of esophagus on barium swallow Spontaneous nonperistaltic (uncoordinated) contractions of esophagus with normal LES pressure Presents with dysphagia and chest pain (angina like). Manometry is diagnostic
Scleroderma	<ul style="list-style-type: none"> Esophageal smooth muscle atrophy → low LES pressure – acid reflux and dysphagia Part of CREST syndrome
Plummer Wilson syndrome	<ul style="list-style-type: none"> Triad of esophageal web, iron deficiency anemia and dysphagia It carries risk of squamous cell carcinoma of esophagus
Esophageal varices	<ul style="list-style-type: none"> Dilated submucosal veins in the lower 1/3rd of the esophagus due to portal hypertension and is an important source of upper GI bleeding (e.g in alcoholics leading to cirrhosis)
Tumors	<ul style="list-style-type: none"> Leiomyoma is the most common benign tumor of esophagus Malignant tumors include; squamous cell CA (most common) and adenocarcinoma Squamous cell carcinoma is more common worldwide- in upper 2/3rd of esophagus. Risk factors include smoking, alcohol, achalasia, hot liquids and caustic strictures Adenocarcinoma is more common in USA- in lower 1/3rd of esophagus. Risk factors are; Chronic GERD, Barret esophagus, obesity or tobacco smoking.

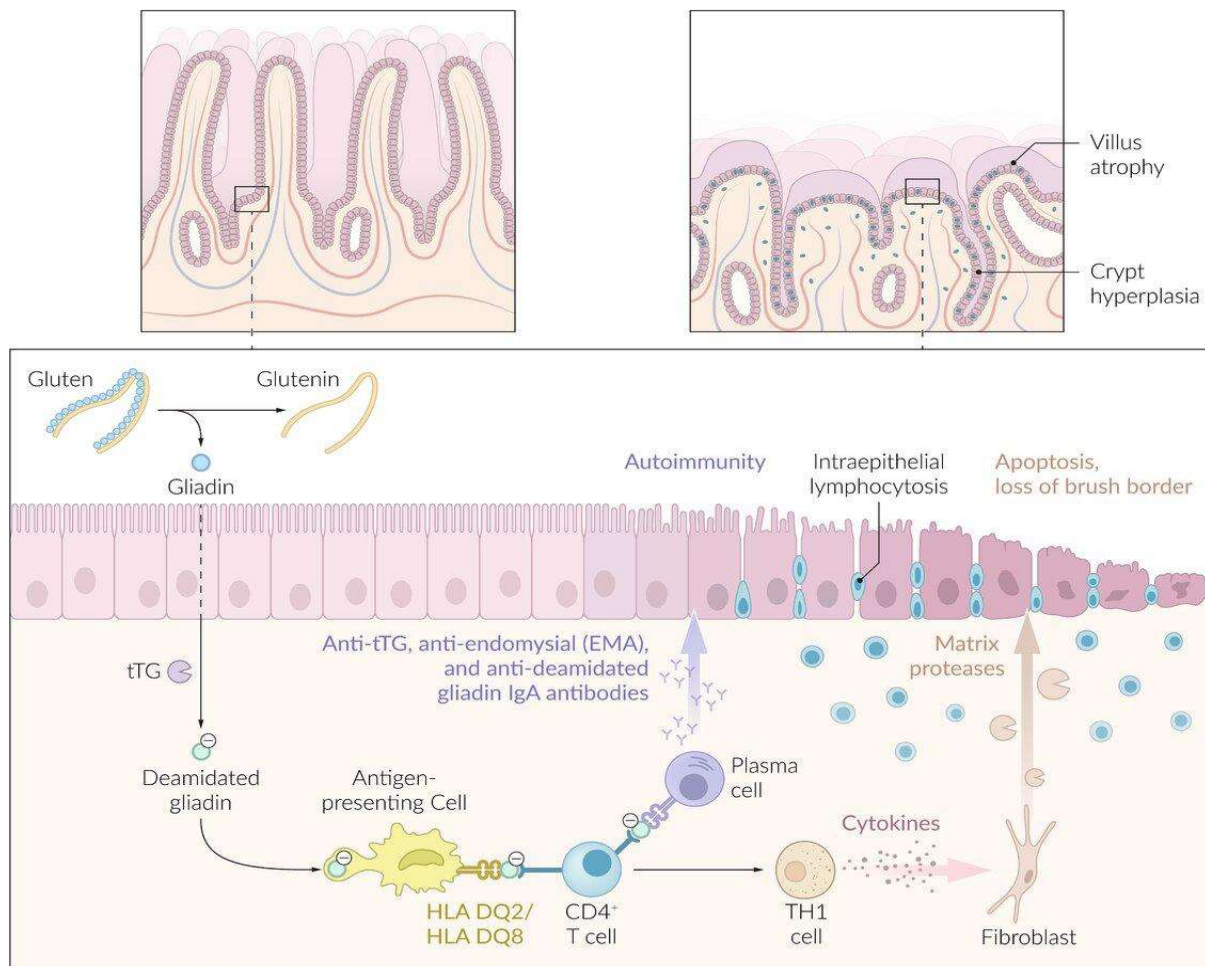
DISEASES OF THE STOMACH

Acute gastritis	Erosions can be caused by: NSAIDS (e.g for rheumatoid arthritis), alcohol, smoking, Burns (curling ulcer), brain injury (cushing ulcer)				
Chronic gastritis	<p>Mucosal inflammation, often leading to atrophy (hypochlorhydria - hypergastrinemia) and metaplasia inc the risk of gastric cancer. Types of chronic gastritis are.</p> <table border="1"> <thead> <tr> <th>Type A chronic gastritis (fundus/body)</th><th>Type B chronic gastritis (antrum/pylorus)</th></tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> Autoimmune cause and affects body/fundus Characterized by autoantibodies to H/K⁺ ATPase on parietal cells and to intrinsic factor that leads to pernicious anemia +achlorhydria Association with type 1 DM, Addison disease, Hashimotos thyroiditis. </td><td> <ul style="list-style-type: none"> H. pylori atrophic gastritis Most common type affects antrum first, then spreads towards body Associated with; gastric/peptic ulcer or gastric MALToma </td></tr> </tbody> </table>	Type A chronic gastritis (fundus/body)	Type B chronic gastritis (antrum/pylorus)	<ul style="list-style-type: none"> Autoimmune cause and affects body/fundus Characterized by autoantibodies to H/K⁺ ATPase on parietal cells and to intrinsic factor that leads to pernicious anemia +achlorhydria Association with type 1 DM, Addison disease, Hashimotos thyroiditis. 	<ul style="list-style-type: none"> H. pylori atrophic gastritis Most common type affects antrum first, then spreads towards body Associated with; gastric/peptic ulcer or gastric MALToma
Type A chronic gastritis (fundus/body)	Type B chronic gastritis (antrum/pylorus)				
<ul style="list-style-type: none"> Autoimmune cause and affects body/fundus Characterized by autoantibodies to H/K⁺ ATPase on parietal cells and to intrinsic factor that leads to pernicious anemia +achlorhydria Association with type 1 DM, Addison disease, Hashimotos thyroiditis. 	<ul style="list-style-type: none"> H. pylori atrophic gastritis Most common type affects antrum first, then spreads towards body Associated with; gastric/peptic ulcer or gastric MALToma 				
Menetrier disease	<ul style="list-style-type: none"> Hyperplasia of surface mucous cells with glandular atrophy → Excess mucous and lack of HCL It is also known as hypertrophic gastropathy and precancerous- can result in malignancy Presents with weight loss, anorexia, vomiting, epigastric pain and edema (due to protein loss) 				

Ulcer	Gastric ulcer <ul style="list-style-type: none"> 70 % - H pylori association other cause- NSAIDs dec mucosal protection against gastric acid Pain increases with meal (weight loss) Inc risk of carcinoma Biopsy of margins to rule out malignancy 	Duodenal ulcer <ul style="list-style-type: none"> 90% H pylori association other cause- Zollinger-Ellison syndrome dec mucosal protection or inc gastric acid Pain decreases with meal (weight gain) Generally, not associated with malignancy Not routinely biopsied
	Peptic ulcer <ul style="list-style-type: none"> Formation of ulcers in any part of GIT, but most commonly 1st part of duodenum involved In stomach: lesser curvature within the antrum (incisura angularis) is the most common location Causes: H pylori (most common), steroids, smoking, inc acid production, NSAIDs, cocaine abuse Endoscopic biopsy is gold standard for diagnosis of peptic ulcer Peptic ulcer has smooth base and non punched elevated margins) Culture is gold standard for H pylori infection. Fecal antigen test is highly sensitive Urea breath test is non-invasive most accurate test, also confirms eradication of H pylori Complications: Hemorrhage (most common), obstruction, perforation (most lethal) 1. Bleeding from gastric ulcer (erosion of left gastric artery) and posterior duodenal > anterior duodenal ulcer. Posterior duodenal ulcer bleeding source is gastroduodenal artery 2. Obstruction of pyloric antrum or duodenum 3. Perforation of anterior duodenal > posterior duodenal ulcer, free air under diaphragm on erect X ray of abdomen with referred pain to shoulder via phrenic nerve irritation 	
Tumors	Adenocarcinoma or intestinal type	<p>Histologically, stomach cancer is almost always adenocarcinoma (intestinal type)</p> <p>Risk factors: H. pylori (most common), smoked fish, meat, nitrosamines, blood group A, Menetrier disease</p> <p>Ulcerated or exophytic lesion (on lesser curvature) that develops into malignancy</p> <p>Necrotic base and raised margins (remember; peptic ulcer has smooth base and non punched elevated margins)</p> <p>It has tendency for early aggressive local spread with nodal/liver metastasis</p> <p>Directly spreads to colon, liver and pancreas</p> <p>Spreads via lymphatics to; left supraclavicular node (Virchow node), periumbilical region (sister Mary joseph nodule) and to ovaries (krukenberg tumor)</p>
	Diffuse gastric cancer	<p>No association with H pylori. E cadherin mutation is responsible, infiltrative growth</p> <p>Stomach wall is grossly thickened and leathery (linitis plastica/plastic bottle like)</p> <p>Signet ring cells i.e mucin filled cells with peripheral nuclei are characteristics</p>
	Other malignancies	<p>Lymphoma, GI stromal tumors (GIST), carcinoid (rare)</p> <p>Gastric lymphoma (MALToma)- H pylori association, treated with antibiotics</p> <p>GIST: derived from pacemaker interstitial cells of Cajal, C-Kit mutation +Ve Imatinib is effective against GIST alongwith surgical resection</p>

Malabsorption Syndromes	<ul style="list-style-type: none"> Disorders of mucosa (celiac disease, Whipple disease, tropical sprue) and digestion e.g lactose intolerance or pancreatic insufficiency. Can be differentiated by D-xylose absorption test Decreased absorption and excretion of D-xylose occurs in intestinal mucosal defects while normal urinary excretion in pancreatic disorders (e.g chronic pancreatitis due to cystic fibrosis) These disorders may cause diarrhea, steatorrhea, weight loss, vitamin & mineral deficiencies Screening for fecal fat e.g Sudan stain and D-xylose absorption need to be done
Celiac disease or sprue	<ul style="list-style-type: none"> Caused by autoimmune mediated sensitivity or intolerance to gluten (in wheat, oat, barley, rye), aka gluten sensitive enteropathy. Associated with HLA-DQ2 and HLA-DQ8 Primarily affects distal duodenum and/ proximal jejunum → malabsorption and steatorrhea

	<ul style="list-style-type: none"> • Jenunal biopsy is gold standard for diagnosis → Histology shows villous atrophy, crypt hyperplasia and intraepithelial lymphocytosis. D-xylose test is abnormal • Serology: anti-endomysial, anti-transglutaminase and anti-gliadin antibodies • Association with other autoimmune disorders e.g type 1 DM and Addison disease • Complications: anemia, weight loss, vitamins and mineral deficiencies, osteoporosis, menstrual irregularities, dermatitis herpetiformis and Inc risk of T cell lymphoma. • Treatment: gluten-free diet, replace vitamins and mineral loss.
Tropical sprue	<ul style="list-style-type: none"> • Disease of unknown cause, seen in residents of or recent visitors to tropics • Similar findings as celiac sprue but responds well to antibiotics • Affects duodenum, jejunum and later on ileum. Associated with folate & B12 deficiency
Whipple disease	<ul style="list-style-type: none"> • Infection with <i>Tropheryma whipplei</i>, common in older age → PAS +Ve foamy macrophages in intestinal lamina propria (on jejunal biopsy), cardiac and neurological symptoms + arthralgia • Diarrhea/steatorrhea occur later in disease. Diagnosis made by tissue PCR • Treatment: IV penicillin + streptomycin for 2 weeks or oral co-trimoxazole/tetracycline for 1 year
Lactose intolerance	<ul style="list-style-type: none"> • Lactase deficiency (brush border enzyme)- intolerance to milk/milk products. Villi appear normal except when secondary to injury at tips of villi (e.g, viral enteritis) • Osmotic diarrhea with low pH of stool (as colonic bacteria ferment the lactose)
Pancreatic insufficiency	<ul style="list-style-type: none"> • Causes malabsorption of fat and fat soluble vitamins (A,D,E,K) as well as Vit B12 • Due to chronic pancreatitis, cystic fibrosis and neoplasm. D-xylose absorption is normal • Decrease fecal elastase and duodenal bicarbonate and pH as well



INFLAMMATORY BOWEL DISEASE		
Chronic inflammatory disease of unknown cause represented by chron's disease and ulcerative colitis		
Characteristics	Chron's disease	Ulcerative colitis
Description	<ul style="list-style-type: none"> May involve entire gut from mouth to anus. Begins from terminal ileum. Rectum is spared. Females > males affected, Th1 mediated. Smoking may trigger CD 	<ul style="list-style-type: none"> Generally, begins in rectum and almost always involves colon. Male = female distribution Th2 mediated Smoking is protective
Morphology (Gross + microscopic)	<ul style="list-style-type: none"> Transmural inflammation Cobble-stone appearance of mucosa Non-caseating granulomas Skip lesions i.e discontinuous fashion 	<ul style="list-style-type: none"> Inflammation limited to mucosa and submucosa. Friable mucosa with superficial/deep ulceration No granulomas and skip lesions Crypt abscess, bleeding, ulcers
Intestinal Features	<ul style="list-style-type: none"> Abdominal pain- right sided occasionally. Diarrhea ± fever, weight loss 	<ul style="list-style-type: none"> Abdominal pain- often lower left sided Bloody diarrhea ± fever, weight loss
Extraintestinal manifestations (rash, eye, arthritis)	<ul style="list-style-type: none"> Aphthous (oral) ulcers Arthritis & skin lesion– most common erythema nodosum Ca+ oxalate renal stones 	<ul style="list-style-type: none"> Arthritis (most common), uveitis Pyoderma gangrenosum Primary Ankylosing spondylitis (p-ANCA +ve) Primary sclerosing cholangitis
Investigations	<ul style="list-style-type: none"> String sign on imaging Anti – Saccharomyces cerevisiae antibody (ASCA – Positive in CD) Colonoscopy with biopsies confirms the diagnosis 	<ul style="list-style-type: none"> Lead pipe appearance Antineutrophil cytoplasmic antibody (ANCA) – Positive in Uc Colonoscopy with biopsies confirms the diagnosis
Complications	<ul style="list-style-type: none"> Peri-anal disease (fissure, anal fistulas) Stricture, abscess, fistulas e.g entero-vesical → recurrent UTIs, pneumaturia Renal stones (Ca oxalate type), gall stone 	<ul style="list-style-type: none"> Fulminant colitis, toxic megacolon and perforation Risk of colorectal cancer is more
Treatment	<ul style="list-style-type: none"> Corticosteroids, azathioprine, antibiotics (e.g., ciprofloxacin, metronidazole), infliximab, adalimumab Use steroids in emergency cases. Azathiopurine for remission 	<ul style="list-style-type: none"> 5-aminosalicylic preparations (e.g., mesalamine), 6-mercaptopurine, infliximab, colectomy 5-ASA compounds for maintenance of remission

Microscopic colitis:

- it is the inflammatory disease of colon seen in old females. Causes chronic watery diarrhea.
- Normal mucosa on colonoscopy, while histology shows inflammatory infiltrate in the lamina propria with thickened subepithelial collagen band or intraepithelial lymphocytosis.

INFLAMMATORY BOWEL DISEASE

Key Points

- ✓ Autoimmune disorders
- ✓ Chronic/remitting intestinal inflammation.
- ✓ Ulcerative colitis —
 - ✓ Mucosa & submucosa
 - ✓ Colon & rectum
- ✓ Crohn's disease —
 - ✓ Transmural
 - ✓ Any segment of GI tract
- ✓ Indeterminate colitis —
 - ✓ 5-15%
- ✓ Diagnosis
 - ✓ Endoscopy
- ✓ Epidemiology & Risk
 - ✓ Teens/early 20s
 - ✓ UC: 2nd peak 60's/70s
- ✓ Genetic factors
 - NOD2 (CD)
- ✓ Environmental
- ✓ Pathogenesis —
 - ✓ Host immune response + intestinal microbiota + intest. barrier defects
- ✓ Neoplasia —
 - ✓ Duration & severity of disease.

Crohn's Disease

Any segment of GI (often ileum & colon; rectum spared)

Th1/Th17-mediated inflammation.

Perianal lesions

Ex: Recto-vaginal fistula

Complications: Fistulas, fissures, obstructive strictures, Dysplasia & adenocarcinoma (less than UC), Anemia (chronic blood loss).

Treatments: Smoking/nicotine cessation, anti-inflammatories, immune suppressors, surgery.

Ulcerative Colitis

Colon & rectum.

Th2-mediated inflammation.

Complications: Toxic ulceritis, toxic megacolon, perforation, Dysplasia & adenocarcinoma (esp. w/pancolitis).

Treatments: Anti-inflammatories, immune suppressors, colectomy.

Extraintestinal CD/UC Manifestations/Complications

Most common: Skin lesions (~40%), Uveitis, Arthritis

Less common: Liver/gallbladder, lung, pancreas, kidneys

Irritable bowel syndrome

- Multifactorial causes (**psychological** stress related/ autonomic nervous system related) without any structural abnormalities. Most common in middle aged females
 - **Diagnostic criteria (Rome-IV criteria)**
 - Recurrent abdominal pain at least 1 day/week in last 3 months associated with ≥ 2 of the following*.
 - (i) Related to defecation (ii). Change in stool frequency (iii). Change in stool consistency/form

* Criteria fulfilled for last 3 months with symptoms onset at least 6 months prior to diagnosis

In Rome-III criteria \rightarrow abdominal pain 3 days/months instead of 1d/week (as in Rome-IV). Rest all same
 - First line management is lifestyle modification and dietary changes
 - **Low FODMAP diet** (low oligosaccharides, disaccharides, monosaccharides, and polyols):
- This type of diet helps avoiding IBS, as given below.

Food	Avoid (High FODMAP)	Use (low FODMAP)
Vegetables	Garlic, onion, peas, cauliflower, mushrooms	Carrot, cucumber, lettuce, potato
Fruits	Apple, mango, berries, cherries, dried fruits, pear, peach	Kiwi, grapes, oranges, strawberries
Dairy products	Milk, condensed milk, soy milk, ice cream, yogurt	Almond milk, lactose free milk, cheese
Protein sources	Marinated or processed meat, poultry/sea foods	Eggs, meat (marinated with olive oil)
Breads & cereals	Wheat/rye/barley breads, biscuits and snack products	Cornflake, oat, rice,
Sugars, sweetener And Nuts/seeds	High fructose corn syrup, honey, carbonated drinks Cashews and pistachios	Dark chocolate, table sugar, maple syrup , Peanuts, walnuts, pumpkin seeds

Diverticulum	<p>Blind pouch protruding from GI tract that communicates with the lumen of gut. Types are; False diverticulum or pseudodiverticulum: only mucosa and submucosa outpouch. Most common in sigmoid colon. Occurs where vasa recta perforate through muscularis externa. Most diverticula e.g (esophagus, stomach, sigmoid colon) are acquired and are termed “false diverticula.” True diverticula: all layers of gut wall outpouch (eg, Meckel).</p> <table border="1" data-bbox="365 331 1425 640"> <tr> <td data-bbox="365 331 544 541">Meckel's diverticulum</td><td data-bbox="544 331 1425 541"> <p>True diverticulum. Persistence of vitelline duct. Mostly asymptomatic Most common congenital anomaly of GI tract The Rule of 2's: 2 inches long, 2 times more common in males, presents in first 2 years of life commonly, 2 feet from ileocecal valve at antimesenteric border of ileum, 2 types of epithelia (gastric/pancreatic) Ectopic GI mucosa bleeds most commonly Diagnosis: ^{99m}Tc-pertechnetate scan for uptake by heterotopic gastric mucosa</p> </td></tr> <tr> <td data-bbox="365 541 544 640">Zenker diverticulum</td><td data-bbox="544 541 1425 640"> <p>Pharyngoesophageal false diverticulum due to herniation of mucosal tissue at Killian triangle between the thyropharyngeal and cricopharyngeal parts of inferior constrictor muscle. Presents with dysphagia, gurgling, foul breath and neck mass</p> </td></tr> </table>	Meckel's diverticulum	<p>True diverticulum. Persistence of vitelline duct. Mostly asymptomatic Most common congenital anomaly of GI tract The Rule of 2's: 2 inches long, 2 times more common in males, presents in first 2 years of life commonly, 2 feet from ileocecal valve at antimesenteric border of ileum, 2 types of epithelia (gastric/pancreatic) Ectopic GI mucosa bleeds most commonly Diagnosis: ^{99m}Tc-pertechnetate scan for uptake by heterotopic gastric mucosa</p>	Zenker diverticulum	<p>Pharyngoesophageal false diverticulum due to herniation of mucosal tissue at Killian triangle between the thyropharyngeal and cricopharyngeal parts of inferior constrictor muscle. Presents with dysphagia, gurgling, foul breath and neck mass</p>
Meckel's diverticulum	<p>True diverticulum. Persistence of vitelline duct. Mostly asymptomatic Most common congenital anomaly of GI tract The Rule of 2's: 2 inches long, 2 times more common in males, presents in first 2 years of life commonly, 2 feet from ileocecal valve at antimesenteric border of ileum, 2 types of epithelia (gastric/pancreatic) Ectopic GI mucosa bleeds most commonly Diagnosis: ^{99m}Tc-pertechnetate scan for uptake by heterotopic gastric mucosa</p>				
Zenker diverticulum	<p>Pharyngoesophageal false diverticulum due to herniation of mucosal tissue at Killian triangle between the thyropharyngeal and cricopharyngeal parts of inferior constrictor muscle. Presents with dysphagia, gurgling, foul breath and neck mass</p>				
Diverticulosis	<ul style="list-style-type: none"> Many false diverticula of colon (commonly sigmoid colon) mostly in people of 60+ years of age Associated with obesity, constipation and diet that is low in fiber content but high fat/red meat Caused by increased intraluminal pressure and focal weakness in colonic wall Often asymptomatic, vague discomfort, may complicate to painless bleeding or diverticulitis. 				
Diverticulitis	<ul style="list-style-type: none"> Inflammation of diverticula with wall thickness. Hematochezia (bleeding) is rare Classically causing left lower quadrant pain (LLQ pain), pain, fever and leukocytosis Complications include; abscess, fistula, obstruction or perforation 				
Hirschsprung's disease or (Congenital megacolon)	<ul style="list-style-type: none"> Failure of neural crest migration associated with loss of function mutation in RET → lack of ganglion cells/enteric nervous plexuses (Auerbach and Meissner plexuses) in distal segment of colon Risk increases with Down syndrome. Neonates present with bilious vomiting, gut distension and failure to pass meconium within 48 hours due to chronic constipation. Normal portion of colon proximal to aganglionic segment is dilated. Explosive expulsion of feces (squirt sign) → empty rectum on DRE Diagnosed by absence of ganglion cells on rectal suction biopsy. Treated with resection of segment 				

Intestinal Obstruction

- Main types of gut obstruction are adhesion, hernia, volvulus and intussusception
 - Obstruction is demonstrated as multiple air fluid levels on supine X-ray of abdomen
- Adhesion:** most common cause of small bowel obstruction. Fibrous bands of scar formed commonly post surgery
 - Volvulus:** Twisting of portion of bowel around its mesentery; may lead to obstruction and infarction. May occur throughout GI tract. Midgut volvulus are more common in infants and children. Sigmoid volvulus are more common older adults (coffee bean sign on X-ray)
 - Hernia:** Most common hernia is indirect inguinal hernia (including females and neonates). Hernial sac may strangulate leading to obstruction
 - Intussusception:** Telescoping of proximal bowel segment into a distal segment, commonly at ileocecal junction
Most commonly it is idiopathic, but may be due to lead point. Majority of cases in infants
Most common pathological lead point in children → Meckel diverticulum, while in adults → intraluminal mass/tumor
Blood supply is compromised, that causes severe crampy abdominal pain with currant jelly (dark red) stools
Patient may draw legs to chest to ease pain
On abdominal examination: sausage shaped mass in right abdomen
Ultrasound/CT may show **target sign**

	Upper GI bleeding (UGIB)	Lower GI bleeding (LGIB)
Definition	Bleeding from esophagus, stomach, and duodenum proximal (above) to ligament of Treitz	Bleeding from distal small bowel, colon, rectum and anal canal Distal (below) to ligament of Treitz
Presentation	Hematemesis (fresh red blood in vomitus) Coffee ground emesis (non active bleed) Melena (black tarry stools) even 50ml blood loss can appear as melena, Hemodynamic instability	Hematochezia (passage of bright red blood from rectum), if brisk and significant → suspect UGIB Abdominal pain or melena (less common) Pallor, hemodynamic instability if massive
Causes	Peptic ulcer - most common cause (H pylori, NSAIDs) Esophagitis and erosions are next common cause. NSAIDs, anti-coagulants and anti-platelet drugs Alcoholism (e.g, Mallory weis tears), malignancy Ask history of ulcer, drugs and alcoholism	Diverticulosis (5-42%), ischemia (6-18%), anorectal causes (hemorrhoids, fissure, fistula), polyp, neoplasm, angiodysplasia*, IBD (2-4%), radiation colitis, unknown cause in 6-23% cases) Majority of source of LGIB is from colorectal causes
Investigation & Management	UGI endoscopy is the investigation of choice. Labs: CBC, LFTs, RFTs, stool R/E for ova & cyst Hemoglobin is poor indicator in acute bleeding, always look for hematocrit in that case USG and CT scan need to be done IV fluids+ Inj risek + transamin + Octreotide Use Telipressin preferably due to bleed by hepatic or GI cause. Prefer Octreotide in IHD For variceal bleeding → Endoscopic band ligation Treat peptic ulcers and other underlying causes	Colonoscopy rules out the cause in most cases Labs: CBC, LFTs, RFTs, stool R/E (for ova & cyst) Iron deficiency anemia in old age should always raise the suspicion of colorectal cancer CT/MTI Angiography (e.g, angiodysplasia) Treat the underlying cause e.g diverticulosis, IBD, ischemia, hemorrhoids or neoplasm etc.

Source of bleeding		Heavy bleeding		Light bleeding	
Upper GI bleeding	Esophagus				
	Stomach				
	Duodenum				
Lower GI bleeding	Colon				
	Sigmoid				
	Rectum				

Bright red blood

Dark red blood

Black blood

Melena

Coffee ground vomitus

Positive fecal occult blood test

Blood clots

Hematochezia may occur

***Angiodysplasia**: tortuous dilation of vessels most often in right-sided colon, commonly in older patients (+ 70 years) associated with end-stage renal disease, vWD or **aortic stenosis**. Confirmed by angiography

Acute Mesenteric Ischemia	<ul style="list-style-type: none"> Critical blockage of intestinal blood flow (often embolic occlusion of SMA) resulting in small bowel necrosis May present with Abdominal pain, red" currant jelly" stools
Chronic Mesenteric Ischemia	<ul style="list-style-type: none"> "Intestinal angina ": atherosclerosis of celiac artery. SMA. Or IMA resulting in intestinal hypoperfusion Findings: postprandial epigastric pain, weight loss due to food aversion
Colonic ischemia	<ul style="list-style-type: none"> Commonly occurs at water-shed zones (splenic flexure, rectosigmoid junction) Findings: Crampy abdominal pain, hematochezia, thumbprint sign on imaging
Necrotizing Enterocolitis	<ul style="list-style-type: none"> Necrosis of intestinal mucosa (commonly terminal ileum and proximal colon) seen in premature, formula fed infants with immature immune system Presents with currant jelly stools, pneumatosis intestinalis, pneumoperitoneum.

TUMORS OF COLON

<u>COLONIC POLYPS</u>	<ul style="list-style-type: none"> Growths of tissue within colon. Generally classified by histological type Grossly classified as flat, sessile, or pedunculated based on protrusion into colonic lumen
Benign Polyps (Non-neoplastic)	<ol style="list-style-type: none"> Hyperplastic polyps: most common type, smaller size, more in rectosigmoid region, may evolve into serrated polyps Inflammatory pseudopolyps: associated with IBD (e.g Ulcerative colitis) Hamartomatous polyps: growth of normal colonic tissue with distorted architecture, solitary lesions, Associated with Peutz-Jeghers syndrome and juvenile polyposis
Potentially malignant (Neoplastic)	<p>They have following forms:</p> <ul style="list-style-type: none"> Tubular adenomas (most common type 75 %) Tubulovillous adenomas (intermediated risk of malignancy) Villous adenomas (high risk of malignancy) – may cause diarrhea and hypokalemia

POLYPOSIS SYNDROME

Familial Adenomatous polyposis (FAP)	<ul style="list-style-type: none"> Autosomal dominant condition characterized by the presence of hundreds to thousands of adenomatous polyps. The germline defect is in the APC gene on chromosome. The risk of malignant transformation approaches 100%
Gardner Syndrome	<ul style="list-style-type: none"> Variant of FAP Characterized by the presence of numerous adenomatous polyps along with osteomas and soft tissue tumors
Turcot syndrome	<ul style="list-style-type: none"> Variant of FAP that is characterized by adenomatous polyps along with tumors of the central nervous system (especially medulloblastoma).
Peutz-Jeghers Syndrome	<ul style="list-style-type: none"> Autosomal dominant syndrome Numerous hamartomas throughout GI tract, along with hyperpigmented mouth, lips, hands, genitalia Associated with increase risk of colorectal, breast, stomach, small bowel, and pancreatic cancers. Colonoscopy every 2 years after age of 25 for evaluation of polyps and polypectomy
Juvenile Polyposis Syndrome	<ul style="list-style-type: none"> Autosomal dominant syndrome in children (typically < 5 years old) Numerous hamartomatous polyps in the colon, stomach, small bowel. Associated with increase risk of CRC
Lynch Syndrome (HNPCC)	<ul style="list-style-type: none"> Autosomal dominant and 80% progress to CRC. Proximal colon is always involved. Associated with endometrial, ovarian, and skin cancers. Can be identified clinically in families using 3-2-1 rule: 3 relatives with lynch syndrome- associated cancers across 2 generations, 1 of whom must be diagnosed before age 50 years.

Colorectal cancer (Adenocarcinoma of rectum and colon)

Risk factors	<ul style="list-style-type: none"> Adenomatous and serrated polyps, inherited multiple polyposis syndromes, Long- standing ulcerative colitis, Genetic factors, smoking, low fiber diet and processed meat (red meat) Most patients are > 50 years old and approx. 25% have family history 20 % cases of sporadic CRC are due to serrated polyps 								
Presentation	<ul style="list-style-type: none"> Ascending colon (right sided): exophytic mass, occult bleeding, Fe deficiency anemia, weight loss Descending colon (left sided): infiltrative mass, colicky pain, partial obstruction, hematochezia 								
Pathogenesis	<ol style="list-style-type: none"> Chromosomal instability pathways: mutation in APC gene causes FAP and most sporadic cases of CRC via adenoma-carcinoma sequence as given; Loss of APC gene from normal colon → colon at risk → KRAS mutation → Adenoma → loss of tumor suppressor genes (TP53, DCC) → Carcinoma Microsatellite instability pathways: mutation of mismatch repair genes (e.g MLH1 & MSH-2) cause lynch syndrome and some sporadic CRC via serrated polyp pathway. Usually leads to right sided cancers 								
Diagnosis	<ul style="list-style-type: none"> Clinically; right sided CRC bleeds (Fe def anemia) while left sided CRC produces obstruction Apple core" lesion seen on barium enema X-ray Unexplained iron deficiency anemia in men or non-menstruating women (Hb <11 g/dl in men < 10 g/dl in female) raises suspicion of CRC CEA tumor marker good for monitoring recurrence, not useful for screening. Colonoscopy: Screen low-risk patients starting at age 50 with Colonoscopy (alternatives include flexible sigmoidoscopy, fecal occult blood testing (FOBT), CT colonoscopy. <ul style="list-style-type: none"> Patients with a first-degree relative who has colon cancer should be screened via colonoscopy at age 40. Or starting 10 years prior to their relative's presentation. 								
Staging of CRC & Management	<table> <tr> <td>Dukes' A</td><td>Carcinoma in situ limited to mucosa or sub mucosa. Amenable to Surgery</td></tr> <tr> <td>Dukes' B</td><td>Invasion through the bowel wall but not involving lymph nodes. Plan: Surgery then radiotherapy</td></tr> <tr> <td>Dukes' C</td><td>Involvement of lymph nodes Plan: Surgery plus chemotherapy & Radiotherapy may be needed</td></tr> <tr> <td>Dukes' D</td><td>Widespread metastases. Surgery to remove the tumor or to bypass an obstructing tumor, Palliative chemotherapy and/or radiotherapy for symptom relief,</td></tr> </table>	Dukes' A	Carcinoma in situ limited to mucosa or sub mucosa. Amenable to Surgery	Dukes' B	Invasion through the bowel wall but not involving lymph nodes. Plan: Surgery then radiotherapy	Dukes' C	Involvement of lymph nodes Plan: Surgery plus chemotherapy & Radiotherapy may be needed	Dukes' D	Widespread metastases. Surgery to remove the tumor or to bypass an obstructing tumor, Palliative chemotherapy and/or radiotherapy for symptom relief,
Dukes' A	Carcinoma in situ limited to mucosa or sub mucosa. Amenable to Surgery								
Dukes' B	Invasion through the bowel wall but not involving lymph nodes. Plan: Surgery then radiotherapy								
Dukes' C	Involvement of lymph nodes Plan: Surgery plus chemotherapy & Radiotherapy may be needed								
Dukes' D	Widespread metastases. Surgery to remove the tumor or to bypass an obstructing tumor, Palliative chemotherapy and/or radiotherapy for symptom relief,								

INTESTINAL POLYPS & COLORECTAL CANCER

Key Points

- ✓ **Polyps** —
 - ✓ Nodules of tissue that project above mucosa.
 - ✓ Most common in the colon.
 - ✓ Usually asymptomatic; may bleed.
- ✓ **Colorectal cancer** —
 - ✓ Top cause of cancer in U.S.
 - ✓ Most arise from adenomas (adenocarcinomas).
 - ✓ Screening at age 45; earlier if family member has cancer or expectation of early onset.
 - ✓ Diagnose with colonoscopy/flexible sigmoidoscopy
 - ✓ Staging: CT scans, physical exam for metastasis.
 - Liver is most common site of distant metastasis.
 - ✓ Risk factors: adenomatous polyps, age 50+, IBD, family history.
 - ✓ S/Sx: blood in stool, abd. pain, iron deficiency anemia.
 - ✓ Treatment: Surgery, poss. chemotherapy/radiation.
 - ✓ Recurrence is common (esp. rectal cancer).

Polyps

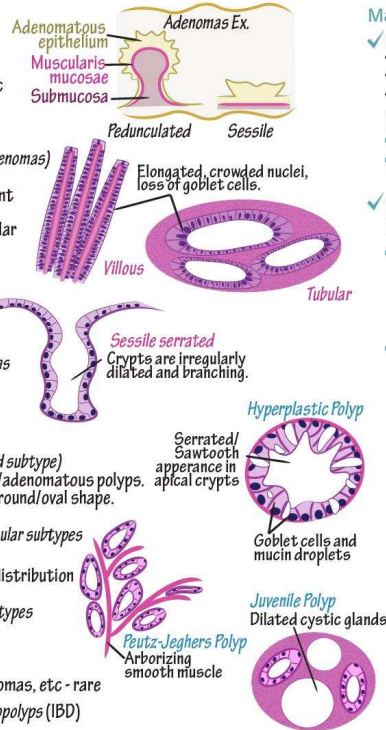
- Morphology: Sessile or Pedunculated
- Neoplastic vs nonneoplastic

Neoplastic

- ✓ **Adenomatous polyps (aka, adenomas)**
 - Very common
 - Size: larger is more malignant
 - Histology: Glandular Villous, Tubulovillous, Tubular
- ✓ **Serrated polyps**
 - Sessile serrated lesions
 - Flat, variable size, mucinous cap.
 - Prox. colon
 - Traditional serrated adenomas
 - Larger; Villous.
 - Distal colon

Nonneoplastic

- ✓ **Hyperplastic polyps (serrated subtype)**
 - Most common; co-exist w/adenomatous polyps.
 - Small (5 mm or less), flat round/oval shape.
 - Distal colon
 - Goblet cell rich & microvesicular subtypes
- ✓ **Hamartomatous polyps**
 - Normal tissue, abnormal distribution
 - Rare, solitary, benign
 - Peutz-Jeghers & Juvenile subtypes
- ✓ **Mucosal polyps (clin. insign)**
- ✓ **Submucosal polyps**
 - Lipomas, leiomyomas, fibromas, etc - rare
- ✓ **Inflammatory polyps & pseudopolyps (IBD)**



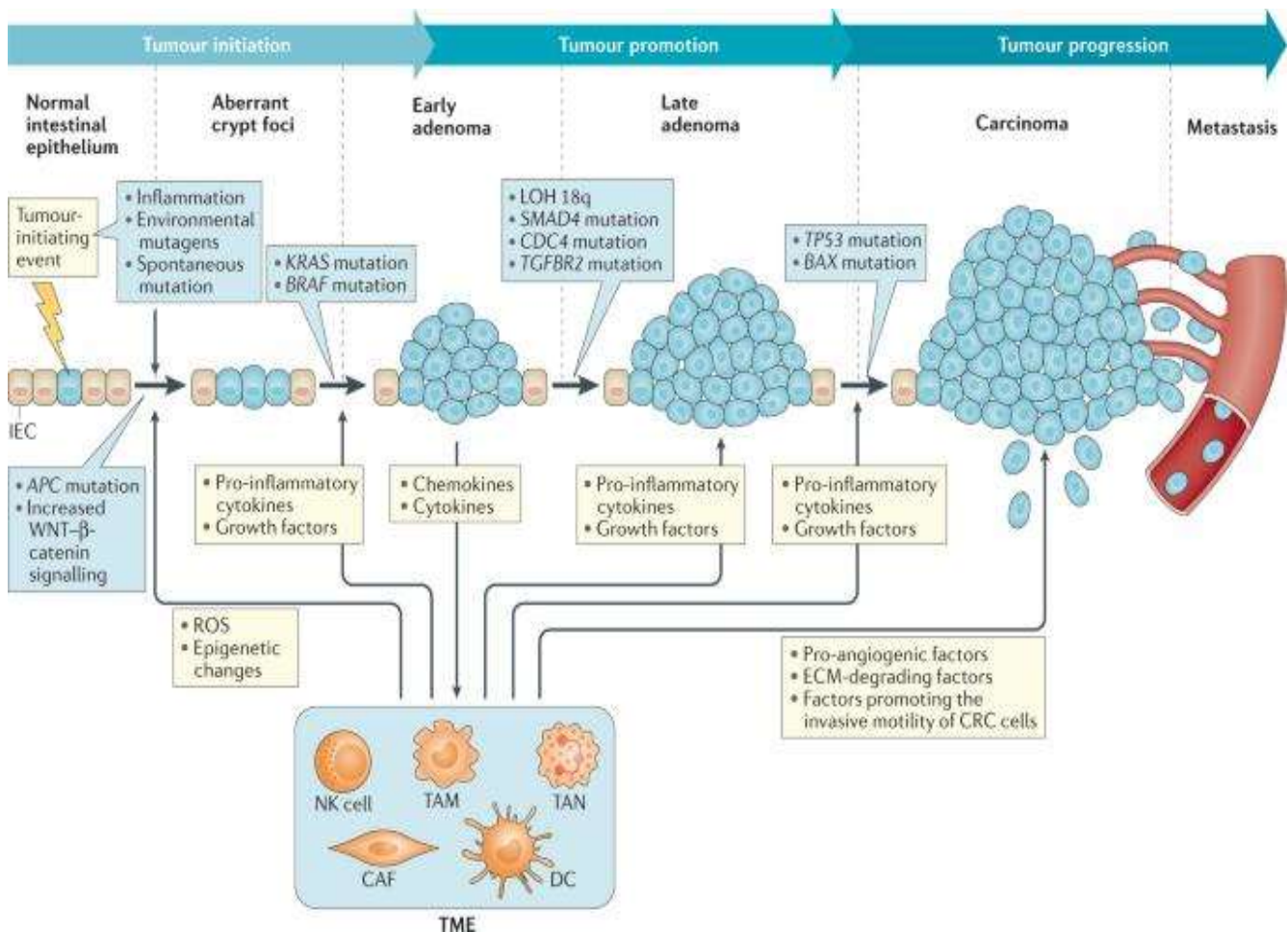
Major polyposis syndromes: Inc. Cancer Risk

- ✓ **Familial adenomatous polyposis:**
 - APC tumor suppressor gene mutation
 - 100s-1000s polyps
 - 100% risk of colorectal cancer
- Extracolonic manifestations:
 - Gardner syndrome: Osteomas, etc.
 - Turcot syndrome: CNS tumors (esp. medulloblastoma)
- ✓ **Hamartomatous polyposis syndromes:**
 - Inherited as autosomal dominant disorders.
 - Peutz-Jeghers Polyposis Syndrome
 - Pigmented macules on mucous membranes & skin.
 - Children: intussusception, torsion, and obstruction.
 - Adults: Cancer (repro & GI)
 - Juvenile Polyposis Syndrome
 - Cutaneous & skeletal manifestations.

Colorectal Cancer

Invasion of submucosa or deeper layers.

- ✓ **Adenocarcinoma pathway**
 - Chromosomal instability: Mutations accumulate over 10-15 years, adenomas progress to invasive carcinomas.
- ✓ **Serrated pathway carcinomas**
 - BRAF/KRAS mutations, Hypermethylation
- ✓ **Lynch syndrome, aka Hereditary nonpolyposis CRC**
 - Most common cause of hereditary CRC.
 - Mismatch repair & microsatellite instability pathway.
 - Early onset and assoc. w/ other cancers - endometrial, liver, brain, etc.



DISEASES OF GI ACCESSORY ORGANS (LIVER, GALLBLADDER & PANCREAS)

<u>JAUNDICE</u>	<ul style="list-style-type: none"> Yellow discoloration of skin, sclera and mucous membranes that gets detectable when serum bilirubin exceeds 3mg/dL Normal bilirubin: Total bilirubin: 0.1 to 1.2 mg/dL (1.71 to 20.5 µmol/L) Direct (conjugated) bilirubin: < 0.3 mg/dL (less than 5.1 µmol/L) On GPE, jaundice is assessed on sclera (in bright light/sunlight), under surface of tongue and extremities (last to appear on palm and soles while first to appear on face region) It may be the only feature of liver disease sometimes (always palpate liver in this case) 				
Type of Jaundice	<ul style="list-style-type: none"> Main types are; Hemolytic jaundice, hepatocellular jaundice and obstructive jaundice Other types are; breastfeeding jaundice, breast milk jaundice and congenital 				
Hemolytic jaundice	<ul style="list-style-type: none"> Unconjugated hyperbilirubinemia (UCB) may be caused by Hemolysis or congenital non hemolytic jaundice Hemolytic jaundice is due to increase production of unconjugated bilirubin (UCB) from hemolysis e.g, sickle cell anemia, hereditary spherocytosis, hemolytic disease of newborn etc. Congenital non-hemolytic anemia: Due to low uptake or decreased conjugation of UCB <table border="1"> <tr> <td>Crigler-najjar syndrome</td><td> <ul style="list-style-type: none"> Crigler-najjar type 1: autosomal recessive, UDP glucuronyl transferase absent. May lead to kernicterus Crigler-najjar type 2: autosomal dominant, UDP glucuronyl transferase decreased, mild jaundice, no kernicterus, treated with oral phenobarbital </td></tr> <tr> <td>Gilbert syndrome</td><td> <ul style="list-style-type: none"> Autosomal dominant. UDP-glucuronyl transferase decreased Occurs in adults in response to stress, alcohol, fasting and strenuous exercise </td></tr> </table> 	Crigler-najjar syndrome	<ul style="list-style-type: none"> Crigler-najjar type 1: autosomal recessive, UDP glucuronyl transferase absent. May lead to kernicterus Crigler-najjar type 2: autosomal dominant, UDP glucuronyl transferase decreased, mild jaundice, no kernicterus, treated with oral phenobarbital 	Gilbert syndrome	<ul style="list-style-type: none"> Autosomal dominant. UDP-glucuronyl transferase decreased Occurs in adults in response to stress, alcohol, fasting and strenuous exercise
Crigler-najjar syndrome	<ul style="list-style-type: none"> Crigler-najjar type 1: autosomal recessive, UDP glucuronyl transferase absent. May lead to kernicterus Crigler-najjar type 2: autosomal dominant, UDP glucuronyl transferase decreased, mild jaundice, no kernicterus, treated with oral phenobarbital 				
Gilbert syndrome	<ul style="list-style-type: none"> Autosomal dominant. UDP-glucuronyl transferase decreased Occurs in adults in response to stress, alcohol, fasting and strenuous exercise 				
Hepatocellular jaundice	<ul style="list-style-type: none"> Due to inability of liver to transport bilirubin into bile, as a consequence of parenchymal liver disease e.g Viral hepatitis Causes mixed hyperbilirubinemia → elevation of both unconjugated + conjugated bilirubin 				
Cholestatic or Obstructive jaundice	<ul style="list-style-type: none"> It causes conjugated hyperbilirubinemia. It may be due to; <ol style="list-style-type: none"> Decreased intra-hepatic bile flow → Primary biliary cirrhosis, Autoimmune hepatitis or congenital conjugated hyperbilirubinemia (Dubin Johnson and Rotor syndrome) <table border="1"> <tr> <td>Dubin- Johnson syndrome</td><td>Defective bilirubin transport Black liver due to dark pigment granules deposition</td></tr> <tr> <td>Rotor syndrome</td><td>Same as Dubin-johnson syndrome but no black liver here</td></tr> </table> Decreased extra-hepatic bile flow → Carcinoma of head of pancreas, Biliary strictures Or Choledocholithiasis (stone in bile duct) 	Dubin- Johnson syndrome	Defective bilirubin transport Black liver due to dark pigment granules deposition	Rotor syndrome	Same as Dubin-johnson syndrome but no black liver here
Dubin- Johnson syndrome	Defective bilirubin transport Black liver due to dark pigment granules deposition				
Rotor syndrome	Same as Dubin-johnson syndrome but no black liver here				
Key Facts	<ul style="list-style-type: none"> Liver function tests (LFTs) include → ALT, AST, ALP, GGT, Serum bilirubin and albumin Marker of structural integrity of hepatocytes → ALT and AST Function of hepatocytes assessed by serum prothrombin and Albumin (normal 3.5-5 mg/dL) Important marker for acute liver failure: serum Prothrombin Marker for chronic liver injury: serum albumin (levels remain almost same in acute liver injury) Test to be done in Hepatic encephalopathy: serum ammonia (NH₃) levels AST is present in mitochondria while ALT is present in cytosol In Viral hepatitis: ALT >> AST raised. Virus causes hepatocyte necrosis Alcohol is a mitochondrial toxin, hence, in alcoholic hepatitis → AST >> ALT raised Both ALP & GGT (more specific) raised in cholestatic jaundice (e.g, bile duct obstruction) ALP is released from liver, bone, placenta and pancreas Test to differentiate jaundice due to intrahepatic or extrahepatic cause → GGT 				

- ❖ **Hepatitis:** discussed in detail in microbiology (virology). Here, Quick recap has been given.
- ❖ Hep A caused by HAV (RNA virus), Orofecal route, no chronic carrier state, 95% cases resolves spontaneously
- ❖ Hep B caused by HBV (DNA virus), parenteral, sexual or vertical transmission, has carrier state (neonates become carrier in 90 % of cases), major risk of HCC (via HBx gene), associated with polyarteritis nodosa, aplastic anemia

- ❖ Hep C caused by HCV (RNA virus), parenteral, sexual or vertical transmission, chronic carrier state, risk of HCC, associated with ITP, autoimmune hemolytic anemia and cryoglobulinemia
- ❖ Hep D caused by HDV (RNA virus), highest fatality rate, requires HBV for infection
- ❖ Hep E caused by HEV (RNA virus), feco-oral route, acute form, no chronicity, highest mortality in pregnancy
- ❖ Mallory bodies (intracytoplasmic, made of intermediate filaments) seen in alcoholic hepatitis

Serological Patterns of Hep-B

Stage	HBsAg	HBsAg	Anti-HBc	Anti-HBs
Acute infection	Positive	Positive	Positive (IgM)	negative
Chronic infection	Positive	Positive	Positive (IgG)	negative
Immune From Previous infection	negative	negative	Positive	Positive
Immune From Vaccination	negative	negative	Negative	Positive
Window Period	negative	negative	Positive (IgM)	negative

- ❖ Immunization for Hep B → 3 doses, at 0, 1 and 6 month, and a booster dose after 5 year
- ❖ Testing for anti-HBs is recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with CKD. Anti-HBs levels should be checked 1-4 months after primary immunization
- ❖ Anti-HBs level (mIU/ml) > 100 indicates adequate response, hence, no further testing required
- ❖ Levels of Anti-HBs (10-100 mIU/mL) indicates suboptimal response → give 1 additional dose of vaccine and no further testing required for immunocompetent individuals
- ❖ < 10 mIU/mL anti-HBs is seen in non responders → test for infection (past/current), give again 3 doses of vaccine course, if still fails to respond – give Hep B immunoglobulins (HBIG) if exposed to virus.

Non-Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Liver Disease (ALD)

NAFLD	<ul style="list-style-type: none"> ❖ Risk factors: Metabolic syndrome (Obesity, insulin resistance, DM, HTN. Hyperlipidemia) ❖ Most common cause of Cryptogenic cirrhosis is NAFLD. There is an increased risk of HCC ❖ ALT > AST raised
ALD	<ul style="list-style-type: none"> ▪ Alcoholic liver disease occurs in 3 forms 1. Alcoholic steatosis (Fatty liver): macrovesicular fatty change reversible with alcohol cessation 2. Alcoholic hepatitis: Long-term consumption causes swollen and necrotic hepatocytes with neutrophilic infiltration. Mallory bodies (intracytoplasmic inclusions of damaged keratin) 3. Alcoholic cirrhosis: Final and usually irreversible form in which Regenerative nodules form, CLD leads to increase portal hypertension and end-stage liver disease. Sclerosis around central vein

<u>LIVER CIRRHOSIS</u>	<ul style="list-style-type: none"> ❖ It is characterized by irreversible diffuse fibrosis with formation of regenerative nodules ❖ Risk for hepatocellular carcinoma (HCC) ❖ Decompensated cirrhosis refers to cirrhosis in association with complications; jaundice, variceal hemorrhage, ascites or encephalopathy and congestive splenomegaly ❖ Liver infarction is unusual as it has dual blood supply
Causes	<ul style="list-style-type: none"> ❖ Viral hepatitis (Hep B + Hep C) is the most common cause worldwide ❖ Alcoholic liver disease (most common) is the most common in west/USA ❖ Primary biliary cirrhosis and sclerosing cholangitis ❖ Autoimmune hepatitis ❖ Wilson disease, α_1-antitrypsin deficiency and non-alcoholic fatty liver disease
Clinical features & complications	<ul style="list-style-type: none"> ❖ Jaundice, asterix (flapping tremors), palmar erythema, spider nevi, gynecomastia. ❖ Hypoalbuminemia caused by decreased albumin synthesis in damaged hepatocytes. ❖ Coagulation factor deficiencies caused by decreased synthesis.

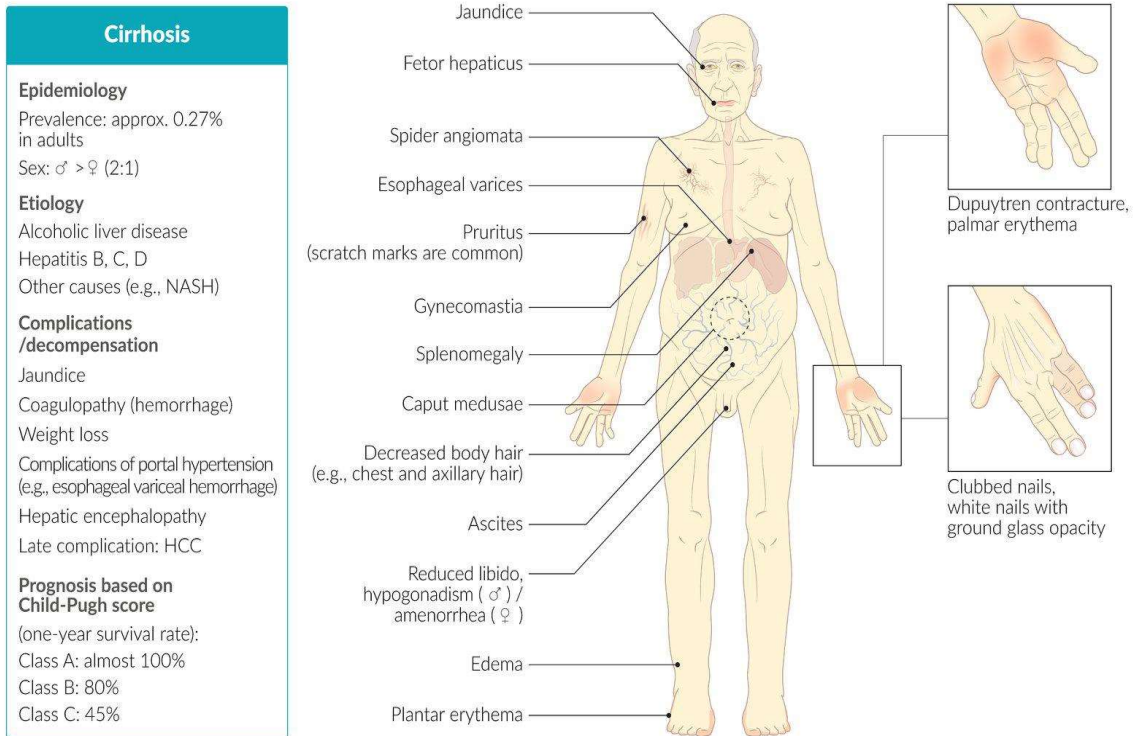
	<ul style="list-style-type: none"> ❖ All coagulation factors (except von Willebrand factor) are synthesized in the liver ❖ Hyperestrinism manifests as palmar erythema; spider nevi (capillary telangiectasia) of face, upper arms, and chest; loss of body and pubic hair, testicular atrophy & gynecomastia ❖ Cirrhosis may cause Portal HTN (ascites, portocaval shunts and variceal bleeding, splenomegaly), hepatic encephalopathy, hepatorenal syndrome and hepatocellular carcinoma
Management	<ul style="list-style-type: none"> ❖ Treat the underlying cause, while, liver transplantation is the definitive treatment

Portal hypertension	<ul style="list-style-type: none"> ❖ BP > 6 mmHg in hepatic region, characterized by the development of venous collaterals with varices in → submucosal veins of the esophagus + hemorrhoidal plexus, and other sites. ❖ it is often classified by the site of portal venous obstruction: ❖ Causes: <ul style="list-style-type: none"> ○ Pre-hepatic: caused by portal and splenic vein obstruction, most often by thrombosis ○ Intrahepatic: caused by intrahepatic vascular obstruction, most often by cirrhosis or Metastatic tumor, and more rarely by exotic entities such as schistosomiasis ○ Post hepatic: caused by venous congestion in the distal hepatic venous circulation, Most often because of constrictive pericarditis, tricuspid insufficiency, congestive heart failure, or hepatic vein occlusion (Budd Chiari syndrome)
Budd-Chiari syndrome	<ul style="list-style-type: none"> ❖ The cause is thrombotic occlusion of the major hepatic veins, resulting in abdominal pain jaundice hepatomegaly ascites, and liver failure. ❖ Budd-Chiari syndrome is most often associated with polycythemia Vera, hepatocellular carcinoma, and other abdominal neoplasms or pregnancy
Congestive Heart Failure	<ul style="list-style-type: none"> ❖ In long-standing chronic right-sided heart failure, the cut surface of the liver can assume appearance of "nutmeg liver," with dark red congested centrilobular areas alternating with pale portal areas. Nutmeg liver = chronic passive hepatic congestion in CHF ❖ Eventually, centrilobular fibrosis may result in cardiac cirrhosis

Hepatic encephalopathy (HE)

Cirrhosis → formation of portosystemic shunts, deranged NH₃ metabolism → neuropsychiatric dysfunction (slurred speech, somnolence, disorientation, coma)

Precipitating factors or triggers	<ul style="list-style-type: none"> • Increase NH₃ production and absorption due to dietary protein. GI bleed, constipation, and infection • Decrease NH₃ removal due to renal failure, diuretics, bypassed hepatic blood flow post -TIPS) 										
Grades of HE	<table> <tr> <td>Grade 0</td><td>Minimal alterations and impairment of executive function</td></tr> <tr> <td>Grade 1</td><td>Drowsy, sleep inversion, irritability, poor concentration</td></tr> <tr> <td>Grade 2</td><td>Lethargy, apathy, and drowsiness</td></tr> <tr> <td>Grade 3</td><td>Stupor, Depressed conscious but arousable</td></tr> <tr> <td>Grade 4</td><td>Coma with no response</td></tr> </table>	Grade 0	Minimal alterations and impairment of executive function	Grade 1	Drowsy, sleep inversion, irritability, poor concentration	Grade 2	Lethargy, apathy, and drowsiness	Grade 3	Stupor, Depressed conscious but arousable	Grade 4	Coma with no response
Grade 0	Minimal alterations and impairment of executive function										
Grade 1	Drowsy, sleep inversion, irritability, poor concentration										
Grade 2	Lethargy, apathy, and drowsiness										
Grade 3	Stupor, Depressed conscious but arousable										
Grade 4	Coma with no response										
Management	<ul style="list-style-type: none"> • Treat the underlying cause if any (e.g, constipation or infection) • Rifaximin 550mg, lactulose (inc ammonia producing gut bacteria) • Correction of hypoglycemia (by 10% dextrose) 										



Cirrhosis

Epidemiology
 Prevalence: approx. 0.27% in adults
 Sex: ♂ > ♀ (2:1)

Etiology
 Alcoholic liver disease
 Hepatitis B, C, D
 Other causes (e.g., NASH)

Complications /decompensation
 Jaundice
 Coagulopathy (hemorrhage)
 Weight loss
 Complications of portal hypertension (e.g., esophageal variceal hemorrhage)
 Hepatic encephalopathy
 Late complication: HCC

Prognosis based on Child-Pugh score
 (one-year survival rate):
 Class A: almost 100%
 Class B: 80%
 Class C: 45%

BACTERIAL PERITONITIS	
Primary or spontaneous Bacterial Peritonitis (SBP)	<ul style="list-style-type: none"> ❖ Complicates ascites, but does not cause it (occurs in 10% of cirrhotic ascites); higher risk in patients with GI bleed. ❖ Presents with fever, chills, abdominal pain, ileus, hypotension, worsening encephalopathy, acute kidney injury ❖ Causative agent: E. coli (most common), Streptococcus or Klebsiella ❖ Diagnosis: Paracentesis with ascitic fluid absolute neutrophil count > 250 cells/mm³.
Secondary Bacterial Peritonitis	<ul style="list-style-type: none"> ❖ Usually results from a perforation of viscera or surgical manipulation. ❖ Most common aerobe is E. coli, while most common anaerobe: Bacteroides

Wilson disease or hepatolenticular degeneration	<ul style="list-style-type: none"> ❖ Autosomal recessive disorder of copper metabolism resulting in accumulation of toxic levels of copper. Normally, copper is absorbed in small intestine, taken into liver, where it is stored and incorporated into ceruloplasmin. • In Wilson's disease: copper incorporation into ceruloplasmin and its excretion into bile are impaired resulting in copper accumulation in liver • Clinical manifestations: <ul style="list-style-type: none"> ○ Liver: hepatitis, fulminant hepatic failure, Micronodular cirrhosis. ○ Eyes: Kayser-Fischer rings (greenish-brown discoloration of cornea) ○ CNS: abnormal movement and behavior, tremors, parkinsonism ○ Decreased serum ceruloplasmin is initial screening test. ↑ urinary excretion of copper is the most accurate test, whereas, liver biopsy is gold standard investigation
Hemochromatosis	Excessive iron storage causing multiorgan system dysfunction (especially Liver, Heart)
Causes	<p>Primary (Hereditary) Hemochromatosis: Most often caused by a mutation in the HFE-gene on chromosome 6</p> <p>Secondary hemochromatosis: Due to Parenteral iron overload (e.g, transfusions). Chronic hemolytic anemia (thalassemia) and Excessive iron intake</p>
Clinical features & complications	<ul style="list-style-type: none"> ○ Mnemonic ABCCDH ○ Arthralgia (any joint, especially MCP joints) ○ Bronze or grey skin (due to melanin, not iron) ○ Cardiomyopathy (dilated), arrhythmias, heart failure ○ Cirrhosis (30%), HCC (200 times increased risk) ○ Diabetes, Hypogonadotropic hypogonadism (impotence, decreased libido, amenorrhea) ○ Hypopituitarism, apathy and other systemic defects
Diagnosis	<ul style="list-style-type: none"> ○ Screening test: Transferrin saturation > 45 % ○ Gold standard: Liver biopsy can be identified on biopsy with Prussian blue stain ○ Genetic testing for hereditary hemochromatosis
Management	<ul style="list-style-type: none"> ○ In symptomatic patients, weekly phlebotomies is the recommended treatment ○ Each 500 ml blood removed contains 200-250 mg iron ○ Aim is to maintain iron <50 and transferrin saturation < 50%
Alpha1 anti-trypsin deficiency	<ul style="list-style-type: none"> ○ Autosomal dominant disorder with deficiency of alpha1 anti trypsin (A1AT) ○ A1AT is a serum protein that is inhibitor of proteases (trypsin and neutrophil elastase) and also component of acute phase reactant produced in acute inflammation ○ Presents with dyspnea, SOB, hepatomegaly, and stigmata of cirrhosis (e.g. gynecomastia) ○ It is the most common cause of childhood cirrhosis (age 3 or 4 years approx.) ○ Complications: Panacinar emphysema, bronchiectasis, neonatal hepatitis Cirrhosis, HCC ○ Diagnosis: measure serum A1AT levels, Panacinar emphysema

DISEASES OF GALL BLADDER AND BILE DUCT

Cholecystitis	<ul style="list-style-type: none"> ❖ Acute or chronic inflammation of gall bladder ❖ Usually from cholelithiasis, most commonly blocking the cystic duct ❖ Acute cholecystitis → fever, Right hypochondrial pain, Murphy sign, raised TLC ❖ Murphy sign-inspiratory arrest on RUQ palpation due to pain. ❖ ↑ ALP if bile duct becomes involved (e.g., ascending cholangitis).
Cholelithiasis (Gallstones)	<ul style="list-style-type: none"> ❖ Risk factors (4 F's): Female, Fat, Fertile (pregnant) and forty (40 years) ❖ Main types of stones: <ol style="list-style-type: none"> 1. Cholesterol stones → often solitary and too large to enter the cystic duct or CBD 2. Pigment stones → due to hemolytic anemia and bacterial infection 3. Mixed stones account for most stones (75% to 80%). Most of these stones are a mixture of cholesterol and calcium salts. can be visualized by USG due to their calcium content ❖ Fatty food intolerance is characteristic ❖ Charcot triad of cholangitis: Jaundice + Fever + right upper quadrant (RUQ) pain ❖ Complications: Biliary colic, pancreatitis, cholecystitis, malignancy
Porcelain Gallbladder	<ul style="list-style-type: none"> ❖ Calcified gallbladder due to chronic cholecystitis; usually found incidentally on imaging ❖ Treatment: prophylactic cholecystectomy due to high risk of gallbladder carcinoma.
Choledocholithiasis	<ul style="list-style-type: none"> ❖ Presence of gallstone or stones in common bile duct ❖ Results in obstructive jaundice with conjugated hyperbilirubinemia, hypercholesterolemia, increased alkaline phosphatase, and hyperbilirubinuria

Biliary tract diseases	<ul style="list-style-type: none"> • Pruritus, jaundice, light-colored stool, dark urine, hepatosplenomegaly • cholestatic pattern of LFTS (↑ conjugated bilirubin, ↑ cholesterol, ↑ ALP)
Primary Sclerosing Cholangitis	<ul style="list-style-type: none"> ❖ It is rare except in association with IBD (especially ulcerative colitis). ❖ Characteristics include inflammation, fibrosis (classically known as "onion skin fibrosis"), and stenosis of intrahepatic and extrahepatic bile ducts. ❖ it develops into biliary cirrhosis and high risk of cholangiocarcinoma
Primary (1°) Biliary cirrhosis	<ul style="list-style-type: none"> ❖ Autoimmune process with Features: Mnemonic: 3M's. <ul style="list-style-type: none"> ○ Most common in Middle-aged women. ○ Anti-Mitochondrial antibodies (in 98% of patients- highly specific) ○ Increase serum IgM Characteristics include severe obstructive jaundice, itching, and hypercholesterolemia: Hypercholesterolemia leads to cutaneous xanthomas ❖ Associated with other autoimmune conditions (e.g. Sjögren syndrome, Hashimoto thyroiditis, CREST, rheumatoid arthritis, celiac disease).
Secondary Biliary cirrhosis	<ul style="list-style-type: none"> ❖ Due to extrahepatic biliary obstruction, bile duct injury & inflammation. ❖ Complications; ascending cholangitis and bacterial inflammation of ducts.

TUMORS OF LIVER & BILIARY TREE		
Benign tumors	<ul style="list-style-type: none"> Hemangioma is the most common benign tumor of liver Hepatic adenoma is related to use of OCPs and it can bleed 	
Malignant tumors	Hepatocellular carcinoma or Hepatoma	<ul style="list-style-type: none"> Most common malignant tumor of liver in adults Associated with HBV strongly and all other causes of cirrhosis (HCV, alcoholic and non-alcoholic fatty liver disease, autoimmune disease, hemochromatosis, α_1-antitrypsin deficiency, Wilson disease) and specific carcinogens (e. g. aflatoxin from <i>Aspergillus</i>). Findings: jaundice, tender hepatomegaly, ascites, polycythemia, anorexia. Spreads hematogenously (via blood) Diagnosis: increase alpha-fetoprotein; ultrasound or contrast CT/MRI, biopsy Triphasic CT scan is investigation of choice Liver transplantation is the definitive treatment
	Hepatic Angiosarcoma	<ul style="list-style-type: none"> Associated with vinyl chloride exposure in factory workers and arsenic in farmers. CT scan is diagnostic
	Cholangiocarcinoma (bile duct carcinoma)	<ul style="list-style-type: none"> Associated with <i>Clonorchis Sinensis</i> (liver fluke), Thorostat exposure, smoking, alcohol and hepatolithiasis Unlike HCC, it is not associated with HBV or cirrhosis

DISEASES OF PANCREAS	
Acute Pancreatitis	<ul style="list-style-type: none"> Due to activation of pancreatic enzymes, resulting in auto digestion of the organ, with hemorrhagic fat necrosis and deposition of calcium soaps, and sometimes formation of pseudocysts (lined by granulation tissue, not epithelium). Causes (GET- SMASHED) <ul style="list-style-type: none"> Gallstones, Ethanol, Trauma Steroids, Mumps, Autoimmune (PAN), Scorpion stings, Hyperlipidemia. / Hypercalcemia ERCP. Drugs (including azathioprine and diuretics). Clinical manifestations include epigastric abdominal pain radiating to back, anorexia, There is an association with increased serum amylase and lipase. Characteristics include hypocalcemia caused by loss of circulating calcium into precipitated calcium-fatty acid soaps.
Chronic Pancreatitis	<ul style="list-style-type: none"> Chronic inflammation, atrophy, calcification of the pancreas Major causes are alcohol abuse and idiopathic. Mutations in CFTR (cystic fibrosis) can cause chronic pancreatic insufficiency. Manifestation: steatorrhea, fat-soluble vitamin deficiency (night blindness, Osteomalacia), diabetes mellitus. Amylase and lipase may or may not be elevated (almost always elevated in acute pancreatitis).
Pancreatic Adenocarcinoma	<ul style="list-style-type: none"> Average survival ~ 1 year after diagnosis, very aggressive tumor Tumors are more common in pancreatic head and cause obstructive jaundice Associated with CA 19-9 tumor marker (also CEA. less specific). Risk factors→ Tobacco use, Chronic pancreatitis (especially > 20 years), Diabetes Presentation: <ul style="list-style-type: none"> Abdominal pain radiating to back, Weight loss Migratory thrombophlebitis-redness and tenderness on palpation of extremities (Trousseau syndrome). Tumors that obstruct the common bile duct result in an enlarged, distended gallbladder; obstructing stones do not (Courvoisier law). Treatment: Whipple procedure, chemotherapy, radiation therapy

PAST PAPERS BCQS

1. Finding in Chron's disease = Perianal disease, oral ulcer, Transmural inflammation, renal stone, cobblestone mucosa on colonoscopy.
2. Hepatitis associated with p-ANCA = Hep B
3. Monitoring of Hepatitis B can be done via = PCR > ALT
4. Prognostic factor to look for developing liver failure = prothrombin time (PT)
5. 45 year old man using analgesic for 3 months for a chronic infection, now complaints of diarrhea and vomiting. On colonoscopy, what can be seen = Fragile submucosa
6. Treated case of Hep A will show on histology = Normal live architecture
7. Alcoholic patient presents with bleeding from hair follicles and non-healing ulcer. Cell line defective is = Fibroblasts
8. Nutmeg liver is = chronic passive hepatic congestion in CHF
9. Pancreatic enzyme deficiency will result in = decrease absorption of TAGs
10. Vitamin produced by intestinal flora and absorbed into blood = Vit K
11. Common location of gastric ulcer = lesser curvature
12. Jejunal biopsy of a 45 year old man shows villous atrophy and PAS +Ve macrophages. Likely diagnosis = Whipple disease
13. Fat malabsorption leads to = steatorrhea
14. Cause of achalasia is = absent myenteric plexus in lower esophagus
15. Ballooning and inflammation of hepatocytes on biopsy of a male that presented with deranged LFTs, the test required = HBsAg
16. Inflammation of portal triads that spills into adjacent lobules, bands of inflammation extending b/w portal areas and terminal hepatic vein with foci of liver necrosis. The diagnosis = Chronic active hepatitis (Piecemeal necrosis is a feature)
17. A 12 year old boy ate chickpeas (chanay) from outside, develops right hypochondrial pain. Likely cause = Hep A
18. Non-healing ulcer in oral cavity of smoker & alcoholic patient is most likely = Squamous cell cancer
19. In CLD, the feature that indicates chronicity = Fibrosis
20. In alcoholic liver disease, microscopic finding = Mallory bodies
21. In CLD, most affected component = Serum Albumin (as it remains normal in acute liver diseases)
22. A patient having HCV +ve, PCR +ve, normal LFTs. What to do next = start interferon & Ribavirin
23. A 20 year old male with h/o foul smelling stool, abdominal cramps and bloating. What is appropriate investigation = Stool DR
24. Most common spread of hepatitis by feco-oral route = Hep E & Hep A
25. Most Lethal/remote area hepatitis in pregnancy = Hep E
26. Common hepatitis in south Asia with least complication = Hep A
27. Most common hepatitis virus transferred by blood transfusion = Hep B (overall most common & fatal is CMV)
28. A lady complaints of worsening dysphagia for 3 months, now difficult for her to swallow pudding/liquid. On examination, lymph nodes of neck are enlarged. The cause is = Esophageal carcinoma (progressive dysphagia from solids to liquids)
29. Test to diagnose Hep B = HBsAg & anti HBc IgM
30. Acute drug induced hepatitis (Quack medicine), will raise = ALT more than AST
31. Chronic drug induced hepatitis (e.g, Hakeem/Quacks medicine) raises = AST
32. Councilman bodies are found in = Yellow fever (hepatitis) > apoptosis
33. Most common cause of raised ALT is = Acute viral hepatitis
34. Appropriate investigation for obstructive jaundice = GGT
35. Neonates commonly have raised bilirubin due to = Hemolysis
36. A patient presented with dark urine, yellow sclera. Test to be done = SGPT & Bilirubin (case of acute viral hepatitis)
37. Presence of delta antigen suggests = Chronicity
38. A known case of cholelithiasis for years now diagnosed with CA gallbladder, the cause = chronic irritation
39. 40 year old female with H/o itching, jaundice, hepatomegaly, xanthoma. The test required for diagnosis = anti mitochondrial antibodies. The diagnosis is Primary biliary cirrhosis – main feature is itching in a middle aged female, jaundice, AMA +Ve

40. A patient of obstructive jaundice starts bleeding due to = Vit K deficiency
41. The cause of non ulcer gastritis is = autoimmune
42. In liver cell injury the enzyme reduced is = Pseudo-cholinesterase > 5 nucleotidase
43. Cause of gastric lymphoma can be = H. pylori
44. Common cause of fatty liver in Pak = Protein deficiency/ Malnutrition
45. Most common cause of HCC = Hep B + Hep C > Hep B
46. Most common cause of cirrhosis = Alcohol
47. Chronic alcoholic with normal LFTs, liver histology may show = Fatty change
48. A 60 year old alcoholic drinker from 15 years presents with deranged LFTs (bilirubin, ALT raised). Histology of liver may show = Piecemeal necrosis (a feature of chronic active hepatitis)
49. Hairy leukoplakia is associated with = EBV in HIV infected
50. A patient presented with hepatitis, viral markers negative, ALT raised. Kayser Fleischer ring on eye exam. Suitable diagnostic test = 24 hour urinary Copper (Wilson disease). Remember, initial test = Serum ceruloplasmin, confirmatory test = 24 hr. Ur Cu
51. Gold standard for Wilson disease = Liver biopsy
52. Severe steatorrhea may result from = Pancreatectomy
53. During pharyngeal phase of swallowing what is true = vocal cords adducted
54. Increase pancreas secretion and calcium levels is by = CCK
55. A patient having Total anti HBc reactive, IgM -Ve, HBsAg -Ve. The diagnosis = Previous/past exposure from Hep B
56. Immune from previous infection of Hep B will show = HBsAg -Ve, HbeAg -Ve, **Anti HBs +Ve, Anti HBc +Ve**
57. **In window** period of Hep B = IgM anti HBc +Ve
58. In case of immunity from vaccination of Hep B = anti HBs +Ve
59. Gastric fundus secretes which of=HCL and intrinsic factor
60. Which of the following neurotransmitter decreases contraction of the stomach & gallbladder =VIP
61. Which hormone responsible for delayed gastric emptying= CCK
62. Na Bile acid transporter is present in= Ileum
63. Most important reflex for defecation=Rectoanal
64. Secretion of HCl by gastric parietal cells is needed for=Activation of pepsinogen to pepsin
65. Enzyme in saliva that presents iron utilization by bacteria= Lactoferrin
66. Oral glucose load will increase which hormone= GIP
67. A single 2cm mass covered by normal intestinal mucosa in a female is likely = Hyperplastic polyp (most common in adults)
68. Newborn presented with jaundice after 2 days of birth = Physiological jaundice
69. Test used to differentiate the type of jaundice = GGT
70. Antibodies to be tested for primary sclerosing cholangitis = anti-neutrophilic cytoplasmic antibodies (p-ANCA), IgM +ve
71. Tumor Marker for HCC = AFP
72. Dysphagia in alcoholic is likely due to = stricture
73. Which of the following is characteristic of saliva as compared to plasma= Hypo tonicity relation to plasma
74. Patient is suspected of pancreatitis with pain in the epigastrium. Histological examination of pancreas shows the cells which are not normally present in the pancreas=Mucous cells
75. Which eating dry fruit saliva becomes= Serous
76. TPN is contraindicated in which of following condition = Liver Disease
77. Mechanism of ascites in CLD = Portal HTN. Edema in cirrhosis is due to = Low albumin
78. Decreased acid in stomach will result in=Abnormal proteins digestion
79. The unconjugated bilirubin is transported in the blood in combination with=Albumin
80. After hepatectomy liver regeneration how many days = 10days
81. Squamocolumnar epithelium present 3 cm above cardiac end of esophagus = Barrett esophagus (above 3 cm)
82. Needle stick injury risk = Hep B (30%) > Hep C (3%) > HIV (0.3 %)
83. Fatty liver develops in alcoholism due to = Acetaldehyde
84. Intrinsic factor secreted by which of following=Fundus of stomach
85. Which hormone responsible for increase intestinal motility = CCK
86. Vagotomy will cause = decreased acid production
87. Surgical removal of the duodenum will enhance = Gastric emptying
88. Best investigation to confirm HCC = Triphasic CT scan liver/Abdomen
89. Sodium is actively absorbing in which part of GIT=Colon

90. Regarding enterokinase true is = Secreted in small intestine convert trypsinogen to trypsin
91. Intrinsic factor is released by = Parietal cell of stomach fundus
92. Pancreatic secretion do not produce which enzyme = Aminopeptidase
93. Strong relation with colon cancer is of = Familial polyposis coli
94. Organism least likely to cause post splenectomy sepsis = E coli. Remember, most common = S pneumoniae
95. Which hormones responsible for increase gastric emptying = Gastrin
96. Most potent stimulator of gastric acid(HCl) = Protein
97. Liver is the only organ involved in synthesis of = Urea formation
98. Highest alkaline PH is present in = Pancreatic secretions
99. Gastrin is produced by = Pyloric antrum
100. Secretin produced by = S cells
101. Substance which relaxes the muscles in lower esophagus, stomach, gallbladder, intestine = VIP
102. Salivary gland secretion increased by = Ach > VIP > Substance P
103. Decrease in gastric secretion by = Somatostatin
104. Role of somatostatin in pancreatic fistula = Decrease secretion
105. Parasite causing bile duct cancer/cholangiocarcinoma = Clonorchis Sinensis
106. Glandular atrophy in stomach of alcoholic/smoker would result in = anemia (Pernicious anemia due to gastric atrophy)
107. Parasympathetic function is = Relaxes GIT Sphincter
108. Contraction in GIT smooth muscle is due to = spontaneous Ca Channel
109. In GIT three layers of muscle on histology = Fundus of stomach
110. Function of somatostatin = Decrease GH secretion
111. Gastric pylorus consists of = Mucous cells
112. A 30 year old man took some injection to inc muscle mass. Over the years, develops acne, icterus, fatigue, hypospemia, Hb 19, Hct 55, PLT and WBC normal. The risk of which neoplasm is high = Hepatocellular carcinoma (likely-androgens induced)
113. Saliva presents iron utilization by microbes via = Lactoferrin
114. Tumor marker for colorectal cancer = CEA
115. Young female develops endometrial cancer. Mother died of same cancer. Brother has CA colon. Gene mutation involved in family = MSH-2, MLH-1 → [Lynch syndrome (cancer of breast, uterus, colon)]
116. Slow waves in small intestine smooth muscles are = Oscillating resting membrane potential
117. Duodenum acidification will lead to = Decrease gastric emptying
118. Jaundice induced by phenobarbital, stress or fasting, the likely cause = Gilbert syndrome
119. Which pancreatic enzyme cause fat digestion = Lipase
120. Activity which push the food forward in esophagus = Primary peristalsis
121. Fat Digestion is done by = Emulsification > Bile salt > HCO₃ & Lipase
122. Atropine inhibits which of the following = Sweat Gland Secretion
123. Parasympathetic action = Opening of GIT Sphincter
124. Most common complication of pancreatitis = Pseudocyst
125. Recurrent facial palsy + fissured tongue = Merkeron Rosenthal syndrome
126. Dietary substance that plays role in esophageal cancer = Nitrosamines
127. To a patient of GERD, what dietary advice you may give = dec fatty diet, avoid soft drinks/hot beverages
128. Most common liver malignancy = Metastasis to Liver [liver metastasis is more common than primary tumors (e.g, HCC)]
129. Which GI Hormone stimulates HCO₃ and water secretion from liver & bile production = Secretin
130. Which of the following antacid decreases gastric emptying = Aluminum hydroxide
131. Which of the following hormone decreases contraction of stomach & gallbladder = VIP
132. Loss of parietal cells due to damage to which of the following area = Fundus
133. Which of the following decreases stomach motility and increases intestinal motility = CCK
134. Enterokinase acts for conversion of = Trypsinogen
135. A man after RTA was transfused blood after few days develops low Hb (8g/dl), On endoscopy, gastritis was found. Likely mechanism involved for gastritis = Bicarbonate and Chloride shift
136. Alcoholic male having raised ALP, GGT 5 times than normal, what will be seen on microscopy = Piecemeal necrosis
137. Mallory bodies are = intracytoplasmic intermediate filaments in alcoholics
138. A male consumes a lot of Pizza, has sedentary lifestyle. Likely to develop = Hypertrophy of steatocytes i.e fatty liver

139. A patient present with anemia post gastrectomy. Which cells of the stomach are likely involved = Parietal cells
140. Production of saliva mainly increased by = parasympathetic stimulation
141. Which of the following increases absorption of iron in the gut = Citrus fruit
142. Cobalamin transported in blood by = Transcobalamin 2
143. Brunner glands are present in = Duodenum
144. Old lady having dysphagia + air fluid level in mediastinum is suffering from = Achalasia
145. Carbohydrates malabsorption is because of absence of = Intestinal lactase
146. Most potent stimulus for Gallbladder contraction = CCK
147. Acute or Severe diarrhea may lead to which acid base abnormality = Metabolic acidosis
148. Chronic diarrhea may lead to = Metabolic alkalosis
149. Baby passes stool after feeding due to which reflex = Gastrocolic reflex
150. Female with h/o Right upper abdominal pain that radiates to tip of shoulder. Likely diagnosis = acute cholecystitis
151. Deficiency of brush border enzyme may lead to = Lactose intolerance (Lactase is brush border enzyme)
152. Likely cause of hepatic adenoma = anabolic steroids (Oxandrolone)
153. Pancreatic secretion compromised. What will happen in relation to absorption and digestion = Failure to digest triglycerides
154. Deficiency of brush border enzyme that cause carbohydrates malabsorption = Lactase
155. Intestinal basic electric rhythm = Does not alter in response to the hormones in circulation
156. CCK which secreted by duodenum cause = Decreases gastric emptying in response to fatty meal
157. Resection of ileum more than 100cm will cause = Dec. Absorption of bile salts
158. Intestinal motility is due to = Spontaneous stimulation of slow wave by Ca^{+}
159. Gastric HCL from parietal cells is needed for = Conversion of pepsinogen to pepsin
160. Highest potential difference in the wall of stomach is when = HCL is not secreted and gastric mucosa is intact
161. Normal waves in basic electrical rhythms of stomach = 3 waves/day
162. Adenocarcinoma of stomach may arise from = Atrophic gastritis
163. Injury 3 finger beneath xiphisternum with episodes of hematemesis. Likely site of lesion = Lower $1/3^{rd}$ esophagus
164. Hep D virus requires what to develop disease = Hep B
165. Risk factor for liver cancer = alcohol, Hep B, Hep C, aflatoxin B1, Wilson disease, hemochromatosis, cirrhosis
166. Pressure on lower esophageal sphincter inc due to = inc gastrin (e.g, by protein diet)
167. Secondary peristalsis due to = Esophagus dilatation
168. CCK and gastrin are similar due to = Same terminal C group
169. During peristalsis when lower esophageal sphincter relaxes = Before bolus reach
170. Secretin is secreted = In response to fatty acids
171. Vagal trunk cut what happens = Incomplete gastric emptying
172. Newborn diagnoses with Hirschprung's disease i.e absence of ganglia. These ganglia receive parasympathetic innervation from S2, S3, S4
173. Which of the following do not causes acid secretion = Acidic antrum
174. Stomach circular muscle become thicker at = Pylorus of stomach
175. In pancreatic fistula somatostatin helps by = Decreasing output of secretions
176. Secretion of gastrin is inhibited by = Somatostatin
177. Substance which induces the flow of saliva = Acetylcholine
178. Regarding GIT motility true is = is not dependent on hormones only
179. Salivation is formed by = Salivary center located in medulla
180. Regarding exocrine pancreatic secretions = Secretion increased by CCK
181. Prostaglandins function in stomach = Decreased parietal cell acid secretion
182. Gastric acid secretion is mediated by = H^+
183. Thick saliva involved which receptors = Alpha 1 Beta 1 receptors mediated
184. Time taken by food to reach large intestine from pylorus = 8 hours
185. Cause of intestinal obstruction having worse prognosis = mesenteric ischemia
186. Artery involved in abdominal angina/mesenteric ischemia (post prandial pain after eating) = SMA
187. RAS mutation is involved in = Colon cancer
188. Malignancy that transfers/spreads through blood relations more = colon cancer (e.g, HNPCC/Lynch syndrome, FAP etc)
189. Enzyme not present in pancreatic secretion = aminopeptidase
190. Which of them is needed to be broken down before digestion = Tripeptides

191. Oligosaccharide in saliva to which microbe adhere to attach to mucosa=Mucin
 192. A young patient presented with jaundice, high ALT, low Hb, inc retic count. Likely cause of jaundice = Hemolysis (raised retic, low Hb). [It may be a case of pigment stones due to hemolysis]
 193. Saliva helps in digestion and it is secreted by= Ach > VIP
 194. Saliva has rich in digesting carbohydrates=Amylase
 195. Which of the following neurotransmitter decreases contraction of stomach & gallbladder=VIP
 196. Enzyme in saliva that prevents iron utilization by bacteria=Lactoferrin
 197. Role of somatostatin in pancreatic fistula is to=Decrease secretion
 198. Pancreatic enzyme deficiency would result in=Decreases absorption of triglycerides
 199. Trypsinogen is activated to trypsin by= Enterokinase
 200. Psuedomyxoma peritonei spreads by = Seeding to other sites/cavities
 201. Patient develops numbness, tingling sensation after total gastrectomy. Likely cause = Vit B deficiency
 202. Fever + jaundice + gallstones detected. What type of stones expected = Pigmented
 203. Major hemostatic defect in CLD = Raised PT
 204. What will be dilated in portal HTN = Left gastric > Left Colic > Right colic
 205. Chagas disease and congenital megacolon affect = Muscularis externa
 206. Patient of hepatitis develops raised ALT & AST. The cause for raised enzymes = Hepatocyte membrane damaged
 207. Part of intestine having thick loop, less fat in mesentery, long vasa recta = Jejunum
 208. A female presented with Dysphagia to liquid for last 6 months. Laryngoscopy shows normal histology of tract the most likely cause = Loss of Neuromuscular co-ordination
 209. Mainly gluconeogenesis occurred at= Liver
 210. Carbohydrates digestion in saliva by= Amylase
 211. Fat digestion done by= Emulsification
 212. Alcoholic male presents with severe epigastric pain radiating to back, nausea, vomiting, fever, raised amylase. The likely diagnosis = acute pancreatitis
-

ENDOCRINOLOGY

Endocrine glands are ductless i.e., they pour their secretions into blood to be carried to effector organs.

Hormones

- Hormones are chemical messengers, synthesized by endocrine glands.
- Based on chemical nature, hormones are classified into three types.

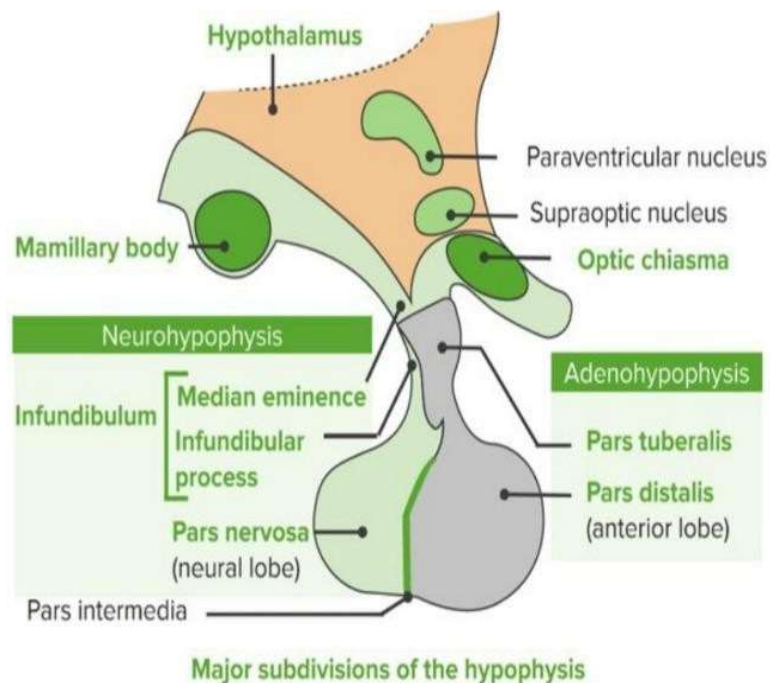
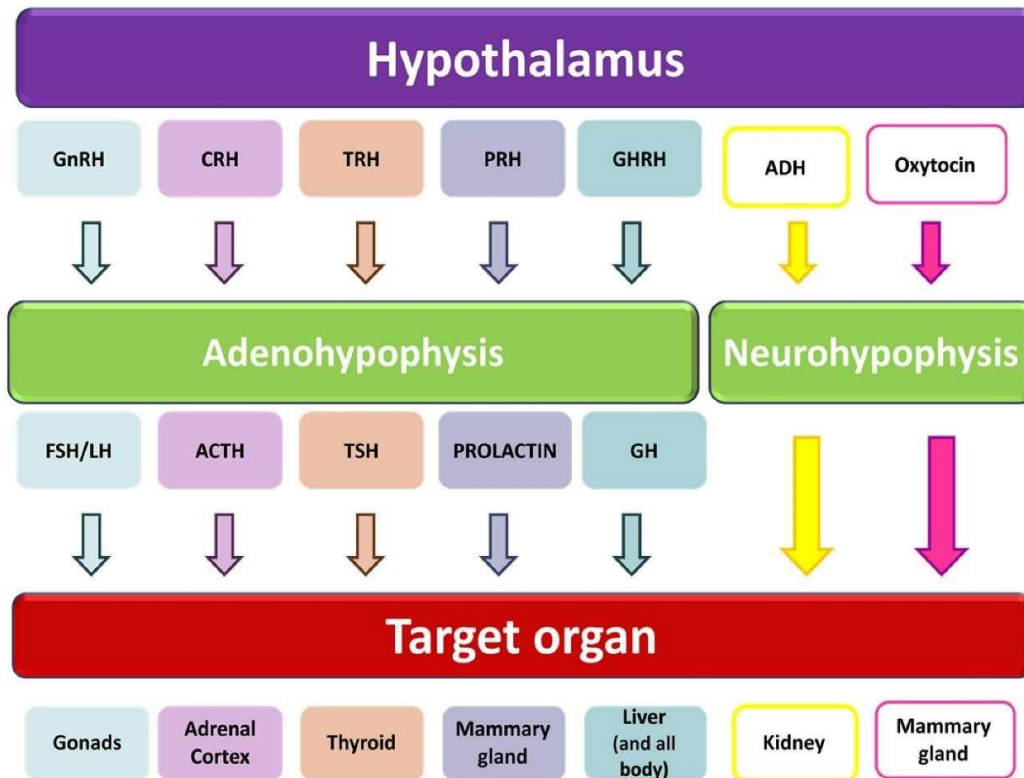
Type of Hormone	Derivative of & Examples
Steroid	Derivative of cholesterol. Examples: Aldosterone, cortisol, testosterone, dihydrotestosterone, estrogen, progesterone
Protein	Formed by ER as Pre-prohormone cleaved into prohormone transported to Golgi apparatus where it is cleaved to form hormone. Examples: FSH, LH, ACTH, TSH, PTH, prolactin, growth hormone, Insulin, Glucagon
Amine derivatives	Derivative of tyrosine. Examples: Thyroxine (T4) and Triiodothyronine (T3) Adrenaline (Epinephrine) Noradrenaline (Norepinephrine) and Dopamine.

Mechanism of action of Hormones

Mechanism	Examples of Hormones
cAMP	PTH, ACTH, MSH, FSH, LH, CRH, ADH, HCG
IP3 & DAG	GnRH, TRH, ADH (V1 receptors), oxytocin, angiotensin-II, Gastrin, histamine (H1)
cGMP	ANP, BNP, NO
Steroid hormone mechanism (Intracellular)	Steroid and thyroid hormones are lipid soluble i.e., they can cross membrane. Intracytoplasmic receptors → steroids e.g, estrogen, progesterone, cortisol, vit D Nucleus → thyroid hormones- retinoid X receptors (RXR)
Tyrosine kinase activation	Insulin, insulin like growth factor-1 (IGF-1), Growth hormone, prolactin

Source	Hormones
Hypothalamus	❖ Thyrotropin-releasing hormone (TRH) ❖ Corticotropin-releasing hormone CRH ❖ Gonadotropin-releasing hormone (GnRH) ❖ Growth hormone-releasing hormone (GHRH) ❖ Somatotropin release-inhibiting hormone (SRIF /somatostatin) ❖ Prolactin-inhibiting factor (PIF/ dopamine)
Anterior Pituitary	❖ Growth hormone (GH) ❖ Thyroid stimulating hormone (TSH) ❖ Adrenocorticotrophic hormone (ACTH) ❖ Follicle stimulating hormone (FSH) ❖ Luteinizing hormone (LH) ❖ Prolactin
Posterior Pituitary	❖ Antidiuretic hormone (ADH) and Oxytocin
Thyroid Gland	❖ Thyroxine (T4), Triiodothyronine (T3) and Calcitonin
Parathyroid Gland	❖ Parathormone (PTH)
Pancreas	❖ alpha cells → Glucagon (peripheral) ❖ Beta cells → Insulin (central) ❖ delta cells → Somatostatin (interspersed)
Adrenal Cortex	❖ Mineralocorticoids → Aldosterone ❖ Glucocorticoids → Cortisol ❖ Sex hormones → Androgens, Estrogen, Progesterone
Adrenal Medulla	❖ Adrenaline (Epinephrine), Noradrenaline (NE) and Dopamine
Testis	❖ Testosterone, Dihydrotestosterone and Androstenedione.

Ovaries	❖ Estrogen and Progesterone
Pineal gland	❖ Melatonin
Thymus	❖ Thymosin and Thymin
Kidney	❖ Erythropoietin, Renin, 1,25-dihydroxycholecalciferol (calcitriol), PGs
Placenta	❖ Human chorionic gonadotropin (HCG) ❖ Human chorionic somatomammotropin, Estrogen and Progesterone



Hypothalamic – Pituitary Hormones

Hormone	Function	Clinical Notes
CHR	<ul style="list-style-type: none"> ↑ ACTH, MSH, B-endorphin 	<ul style="list-style-type: none"> Decreased in chronic exogenous steroid use
Dopamine	<ul style="list-style-type: none"> Decreases Prolactin, TSH 	<ul style="list-style-type: none"> Dopamine antagonists (e.g, antipsychotics) can cause galactorrhea due to hyperprolactinemia.
GHRH	<ul style="list-style-type: none"> ↑ GH 	<ul style="list-style-type: none"> Analog (tesamorelin) used to treat HIV- associated lipodystrophy
GnRH	<ul style="list-style-type: none"> ↑ FSH, LH 	<ul style="list-style-type: none"> Suppressed by hyperprolactinemia. Tonic GnRH suppresses HPG axis. Pulsatile GnRH leads to puberty, fertility
Prolactin	<ul style="list-style-type: none"> Decreases GnRH 	<ul style="list-style-type: none"> Pituitary prolactinoma → amenorrhea, Osteoporosis, hypogonadism. galactorrhea
Somatostatin	<ul style="list-style-type: none"> Decreases GH, TSH 	<ul style="list-style-type: none"> Analog (e.g. Octreotide) used to treat acromegaly.
TRH	<ul style="list-style-type: none"> ↑ TSH, prolactin 	<ul style="list-style-type: none"> ↑ TRH (e.g., in 1°/2° hypothyroidism) may increase prolactin secretion → galactorrhea

Ant. Pituitary (adenohypophysis)	Post. Pituitary (neurohypophysis)
<ul style="list-style-type: none"> ❖ Ectodermal in origin and arises from Rathke's pouch ❖ Hormones from hypothalamus are transported to anterior pituitary through Hypothalamo hypophyseal portal tract system 	<ul style="list-style-type: none"> ❖ Neuroectodermal in origin and arises from hypothalamus. ❖ Hormones from hypothalamus to posterior pituitary are transported by nerve fibers i.e hypothalamo-hypophyseal tract

Hormones of Pituitary Gland

Ant. Pituitary	<p>(FLAT PIG) FSH, LH, ACTH, ISH, Prolactin and GH FSH, LH, ACTH and TSH</p> <p><u>Growth hormone (Somatotropin):</u></p> <ul style="list-style-type: none"> ❖ Homologous with prolactin and human placental lactogen ❖ Growth hormone is released in pulsatile fashion. ❖ <u>Secretion is Increased by:</u> <ul style="list-style-type: none"> ○ Hypothalamus via GHRH stimulates the synthesis and secretion of growth hormone ○ Secretion is increased by hypoglycemia > Exercise > Sleep (NREM) ○ <u>Secretion is decreased by:</u> <ul style="list-style-type: none"> Somatostatin (inhibits secretion of growth hormone by blocking the response of the anterior pituitary to GHRH), Somatomedins (it inhibits the secretion of growth hormone by acting directly on the anterior pituitary and by stimulating the secretion of somatostatin from the hypothalamus.), Obesity, hyperglycemia, and pregnancy. ❖ Action: Decrease glucose uptake (diabetogenic). ↑ lipolysis. ↑ protein synthesis in muscle-inc lean body mass <p>2. <u>Prolactin:</u></p> <ul style="list-style-type: none"> ❖ Secretion is increased by estrogen (OCPS, pregnancy), breast feeding, dopamine antagonists (most antipsychotics). ❖ Secretion is decreased by dopamine, Dopamine agonists (e.g., bromocriptine-can be used in treatment of prolactinoma) and by prolactin itself via negative feedback ❖ Actions: Milk production and breast development (along with estrogen). GnRH spermatogenesis and ovulation)
Posterior Pituitary	<p><u>Antidiuretic hormone (ADH):</u></p> <p>Origin :from supraoptic nuclei of hypothalamus.</p> <p>Secretion is increased by ↑ Serum osmolarity. Volume contraction. Nausea is the most potent stimuli.</p> <p>Secretion is decreased by ↓ Serum osmolarity and Ethanol</p> <ul style="list-style-type: none"> ❖ Action is to ↑ the H₂O permeability of the late distal tubules and collecting ducts ↑ H₂O absorption less water in urine (concentrated urine). ❖ ADH is a powerful vasoconstrictor and maintains blood & ECF volume <p><u>Oxytocin (Love hormone)</u></p> <ul style="list-style-type: none"> ❖ Originates in the paraventricular nuclei of the hypothalamus.

	<ul style="list-style-type: none"> ❖ Regulation: Suckling, sight, and sound of the baby releases oxytocin ❖ Actions: Ejection of milk and Contraction of uterus during pregnancy (Oxytocin can be used to induce labor and reduce postpartum bleeding)
--	---

THYROID GLAND

- ❖ Thyroid hormones are tri-iodothyronine (T3) and thyroxine (T4)
- ❖ Transported in blood by combining with plasma proteins, most of which is bound to thyroxine-binding globulin (TBG)
- ❖ T4 is 90% and T3 is 10%.
- ❖ T4 is converted to T3 by iodine
- ❖ T3 is more active than T4.
- ❖ Composed of
 - Follicles → major constituent of which is thyroglobulin that contains thyroid hormones
 - Parafollicular (C) cells → present b/w thyroid follicles which secrete calcitonin, concerned with calcium metabolism.

Formation	<ul style="list-style-type: none"> ❖ 4 steps 1. Thyroglobulin is synthesized from tyrosine in the thyroid follicular cells, 2. Iodide trapping / iodide pump/ Na- I cotransport Active transport of iodide into thyroid follicular cells is called iodide trapping for incorporation into thyroid hormones. It is inhibited by thiocyanate. 3. Oxidation of iodide (I⁻) to iodine (I₂) Accelerated by peroxidase enzyme and inhibited by propylthiouracil. 4. Organification of I₂: <ul style="list-style-type: none"> • Tyrosine + I₂ mono-iodotyrosine (MIT) • MIT + I₂ di-iodotyrosine (DIT) • MIT+DIT → tri-iodothyronine (T₃) • DIT+ DIT → tetra-iodothyronine (T₄ or thyroxine) <p>In Hepatic Failure: plasma proteins ↓. TBG ↓ → ↓ total thyroid hormones, but normal levels of free hormone</p> <p>In Pregnancy: TBG ↑ → ↑ total thyroid hormone, but normal levels of free hormones (i.e. clinically euthyroid)</p>
Regulation	<ul style="list-style-type: none"> ❖ Hypothalamus secretes TRH → which acts on ant. Pituitary which release TSH → acts on thyroid releases T3 and T4 → which in turn inhibits TSH secretion by acting on ant. Pituitary.
Action	<ul style="list-style-type: none"> ❖ Bone formation (along with growth hormone), bone maturation ❖ Thyroxine converts chondrocytes into osteocytes. ❖ CNS maturation (deficiency causes mental retardation). ❖ Sympathetic effect → ↑ HR and stroke volume (high output heart failure). ↑ BMR. ❖ ↑ Gluconeogenesis. ↑ glycogenolysis. ↑ lipolysis ❖ The overall effect is catabolic-so as to meet the increase body requirement.

ADRENAL GLAND HORMONES

- ❖ Lies at superior poles of two kidneys. It is divided into adrenal cortex and adrenal medulla.
- ❖ Adrenal cortex → derived from mesoderm Outer portion → 80% of gland.
- ❖ Adrenal medulla → derived from neural crest → inner portion → 20% of gland.

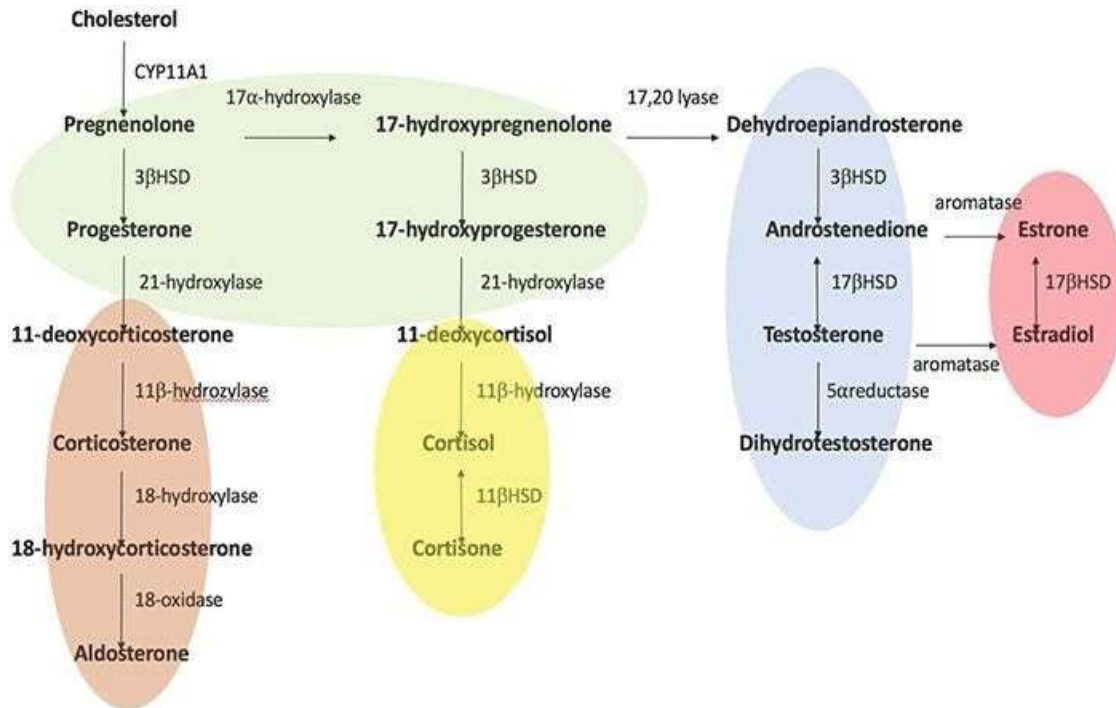
Adrenal Cortex (Adrenocortical Hormones)

- ❖ Adrenocortical hormones are steroids in nature, hence the name 'corticosteroids'. Based on their functions, corticosteroids are classified into three groups:
 1. Mineralocorticoids
 2. Glucocorticoids
 3. Sex hormones (androgens).
- ❖ Consist of 3 layers from outside to inside.
- ❖ Mnemonic: GFR corresponds with Salt (mineralocorticoids), Sugar (glucocorticoids), and Sex (androgens). "The deeper you go, the sweeter it gets."

Parts	Hormone Class	Hormone Produced
Zona Glomerulosa	Mineralocorticoids	Aldosterone
Zona Fasciculata	Glucocorticoids	Cortisol
Zona Reticularis	Androgens	DHEA (dehydroepiandrosterone), Androstenedione.

Synthesis of Adrenocortical hormones

All adrenocortical hormones are steroid in nature and are synthesized mainly from cholesterol precursor



Enzyme Deficiency	Mineralocorticoids	cortisol	Sex hormones	BP	K+	Labs	Presentation
17a- hydroxylase	↑	↓	↓	↑	↓	↓ Androstenedione	XY: ambiguous genitalia, undescended testes XX: lacks 2° sexual development
21-hydroxylase	↓	↓	↑		↑	↑ Renin Activity ↑ 17-Hydroxyprogesterone	Most common Presents in infancy (salt wasting) or childhood (precocious puberty) XX: virilization
11-β hydroxylase	↑ aldosterone + 11-deoxycorticosterone (results in ↑ BP)	↓	↑	↑	↓	↓ Renin Activity	XX: virilization

Adrenal Cortex Hormones

Mineralocorticoids (Aldosterone)	Glucocorticoids (Cortisol)						
Act on the minerals (electrolytes), particularly sodium and potassium	Exhibits circadian rhythm (24-hour periodicity) → For those who sleep at night Cortisol levels are highest just before waking (8 am) and lowest in the evening (approx. 12 midnight)						
Regulation	Regulation						
<ul style="list-style-type: none">• ACTH• Renin-angiotensin-aldosterone system ↓ECF Volume → ↓ renal perfusion pressure activates renin secretion.<ul style="list-style-type: none">○ Renin causes conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin- converting enzyme (ACE).○ Angiotensin II → ↑ aldosterone.○ Aldosterone increases renal Na+ reabsorption, thereby restoring extracellular fluid (ECF) volume and blood volume to normal.❖ <u>Hyperkalemia</u><ul style="list-style-type: none">○ It ↑ aldosterone secretion. Aldosterone ↑ renal K+ secretion, restoring serum (K+) to normal.○ K+ ions is the most effective stimulant for aldosterone secretion.	<ul style="list-style-type: none">○ Hypothalamic-pituitary-cortex relationship or hypothalamic - pituitary-adrenocortical axis (HPA axis)○ Hypothalamus release CRH, that acts on Anterior pituitary releases ACTH→ which acts on all zones of adrenal cortex and along with other hormones also ↑ cortisol level❖ Negative feedback control by cortisol<ul style="list-style-type: none">○ Excess Cortisol level inhibits the secretion of CRH from the hypothalamus and the secretion of ACTH from the anterior pituitary by negative feedback○ The dexamethasone suppression test is based on the ability of dexamethasone (a synthetic glucocorticoid) to inhibit ACTH secretion.○ Test variants. <table><tr><th>Normal Persons</th><th>ACTH-Secreting Tumors</th><th>Adrenal Cortical Tumors</th></tr><tr><td>Low-dose dexamethasone inhibits ACTH and cortisol secretion.</td><td>Low-dose dexamethasone does not inhibit cortisol secretion but high-dose dexamethasone does inhibit</td><td>Neither low- nor high-dose dexamethasone inhibits cortisol secretion.</td></tr></table>	Normal Persons	ACTH-Secreting Tumors	Adrenal Cortical Tumors	Low-dose dexamethasone inhibits ACTH and cortisol secretion.	Low-dose dexamethasone does not inhibit cortisol secretion but high-dose dexamethasone does inhibit	Neither low- nor high-dose dexamethasone inhibits cortisol secretion.
Normal Persons	ACTH-Secreting Tumors	Adrenal Cortical Tumors					
Low-dose dexamethasone inhibits ACTH and cortisol secretion.	Low-dose dexamethasone does not inhibit cortisol secretion but high-dose dexamethasone does inhibit	Neither low- nor high-dose dexamethasone inhibits cortisol secretion.					

Actions/Effects	Actions/Effects
<ul style="list-style-type: none"> ❖ ↑ Renal Na⁺ reabsorption (via principal cells) ❖ ↑ Renal K⁺ secretion (via principal cells) ❖ ↑ Renal H⁺ secretion (via alpha-intercalated cells) 	<p>Anabolic to liver but catabolic to peripheral tissues Cortisol is a A BIG FIB.</p> <ul style="list-style-type: none"> ❖ ↑ Appetite ❖ ↑ Blood pressure: Upregulates α₁-receptors on arterioles → ↑ sensitivity to vasoconstrictor effect of norepinephrine ❖ ↑ Insulin resistance (diabetogenic) ❖ ↑ Gluconeogenesis, lipolysis, and proteolysis (i.e. ↓ glucose utilization) ❖ ↓ Fibroblast activity (poor wound healing, ↓ collagen synthesis, striae) ❖ ↓ Inflammatory and Immune responses: <ul style="list-style-type: none"> ○ Inhibits production of leukotrienes and prostaglandins ○ Blocks histamine release from mast cells ○ Blocks IL-2 production ❖ ↓ Bone formation (↓ osteoblast activity) ❖ Earliest hormone released in stress (e.g surgery) is: CRH (earliest) → ACTH (2nd) → Cortisol → Hyperglycemia <p>Remember the 4 main stress hormones: Cortisol, glucagon, epinephrine, growth hormone</p>

ENDOCRINE PANCREAS

	Insulin (Anabolic)	Glucagon (Catabolic)
Source	Beta cells of pancreas	Alpha cells of pancreas
Mechanism	Receptor Tyrosine kinase	cAMP
Stimulus for secretion	<ul style="list-style-type: none"> ❖ ↑ Blood glucose ❖ ↑ Amino acids ❖ ↑ Fatty acids ❖ Glucagon, Growth hormone, Cortisol ❖ GIP 	<ul style="list-style-type: none"> ❖ ↓ Blood glucose ❖ ↑ Amino acids ❖ CCK, NE, epinephrine, ACh
Actions	<ul style="list-style-type: none"> ❖ ↑ glucose uptake into cells and glycogen formation ❖ ↓ glycogenolysis and gluconeogenesis ❖ ↑ protein synthesis ❖ ↑ fat deposition and decreases lipolysis. ❖ Increases K⁺ uptake into cells 	<ul style="list-style-type: none"> ❖ catabolic- overall ❖ ↑ Glycogenolysis ❖ ↑ Gluconeogenesis ❖ ↑ Lipolysis and Ketoacid Production
Overall effect (blood levels)	<ul style="list-style-type: none"> ❖ ↓ Glucose ❖ ↓ Amino Acid ❖ ↓ Fatty Acid ❖ ↓ Ketoacid ❖ Hypokalemia 	<ul style="list-style-type: none"> ❖ ↑ Glucose ❖ ↑ Fatty Acid ❖ ↑ Ketoacid

D cells secrete Somatostatin → Inhibits secretion of insulin, glucagon, and gastrin

Key facts

Insulin- Mode of Action:

- Rapid action is entry of K into cell. Intermediate action is stimulation of proteins.
- late action is mRNA synthesis for lipogenesis.

Brain vs. RBC's

- Brain utilizes glucose for metabolism normally and ketone bodies during starvation.
- RBCs utilize glucose because they lack mitochondria for aerobic metabolism.

❖ Insulin-Independent Glucose Uptake:

- ❖ Mnemonic: BRICK-L (Brain, RBCs, Intestine, Cornea, Kidney, Liver)

The factors which increase insulin would decrease glucagon and vice versa.

Both functions opposite to each other.

Insulin down regulates its own receptors in target tissue i.e., Insulin receptors are ↑ in starvation, while ↓ in obesity (type 2 DM)

- ❖ **Stimuli for decreased Insulin** → low blood glucose, somatostatin, NE, epinephrine, beta blockers, low K⁺
- ❖ **Stimuli for increased insulin** → inc blood glucose, Fatty acids, amino acids, GLP-1, gastrin, secretin, CCK
- ❖ Most potent hyperglycemic hormone is Glucagon (via glycogenolysis)
- ❖ Cortisol raises blood sugar by gluconeogenesis.

PARATHYROID HORMONE (PTH)

Source	Synthesized and secreted by chief cells of parathyroid gland
Regulations	<ul style="list-style-type: none"> ❖ ↓ serum Ca²⁺ → ↑ PTH secretion and vice versa ❖ ↑ serum PO₄ → ↑ PTH secretion ❖ ↓ Serum Mg²⁺ → ↑ PTH ❖ ↓ ↓ Serum Mg²⁺ → ↑ PTH secretion. Severe hypomagnesemia increase the PTH levels.
Actions	<ul style="list-style-type: none"> ❖ ↑ Bone resorption and kidney reabsorption (at distal convoluted tubules) of Ca²⁺ ❖ ↑ Bone resorption of PO₄. reabsorption of PO₄, In kidneys PCT. ❖ ↑ 1,25-(OH)₂ D₃ (calcitriol) production by stimulating kidneys. ❖ Overall effect: <ul style="list-style-type: none"> ○ ↑ Serum Ca²⁺ (major hormone for regulation of Ca²⁺) ○ ↓ Serum PO₄ and urine PO₄. ○ Mnemonic: (PTH) Phosphate Trashing Hormone

Calcitonin

Source	Para follicular cells (C cells) of thyroid.	❖ Calcitonin opposes actions of PTH.
Regulations	↑ serum Ca ²⁺ calcitonin secretion	❖ Not Important in normal Ca ²⁺ homeostasis
Actions	<ul style="list-style-type: none"> ↓ Bone resorption of Ca²⁺. ↓ Serum Ca²⁺ and keeps it in bones. 	

Vitamin D

Source	Sun, fish, cheese	❖ Inactive forms: <ul style="list-style-type: none"> • Cholecalciferol • 25 hydroxycholecalciferol • 24,25 hydroxycholecalciferol
Regulations	<ul style="list-style-type: none"> ❖ ↑ PTH, serum Ca²⁺, ↓ serum PO₄ ↑ 1,25-(OH)₂ D₃ ❖ ↑ 1,25-(OH)₂ D₃ Inhibits Its own production by negative feedback 	<ul style="list-style-type: none"> ❖ Active form: 1,25-(OH)₂ D₃ ❖ Converted to its active form in kidneys by 1α-hydroxylase.
Actions	<ul style="list-style-type: none"> ❖ ↑ absorption of Intestinal as well as renal Ca²⁺ and PO₄, enhances bone mineralization 	<ul style="list-style-type: none"> ❖ Deficiency causes <ul style="list-style-type: none"> • In children's → Rickets • In adults → Osteomalacia

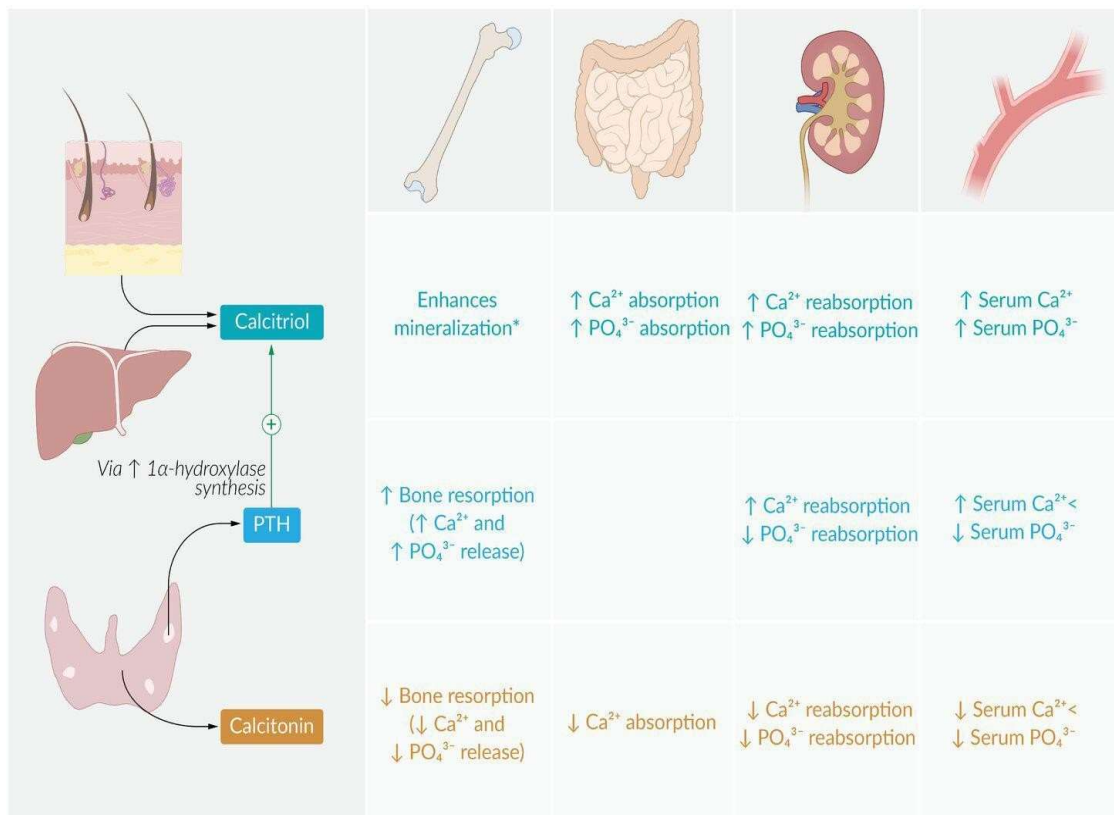
Calcium Homeostasis

- ❖ 40% of total calcium → bound to plasma proteins (albumin).
- ❖ 60% of total calcium → not bound to proteins free/ionized calcium, which is active form.

Normal Ca^{2+} balance	Positive Ca^{2+} balance	Negative Ca^{2+} balance
❖ Normal phenomena	❖ Seen in growing children	❖ in pregnancy and lactation
❖ Intestinal absorption = urinary excretion	❖ Intestinal Ca^{2+} absorption more than urinary excretion.	❖ Intestinal Ca^{2+} absorption less than urinary excretion
	❖ Excess calcium is stored in growing bones	❖ Deficit comes from maternal bones

Summary

PTH	↑ Serum Ca^{2+} , ↓ PO_4 .
Vitamin D	↑ Serum Ca^{2+} , ↑ PO_4 .
Calcitonin	↓ Serum Ca^{2+}



DISORDERS OF ENDOCRINE GLANDS**PITUITARY GLAND****Anterior Pituitary (Adenohypophysis)**

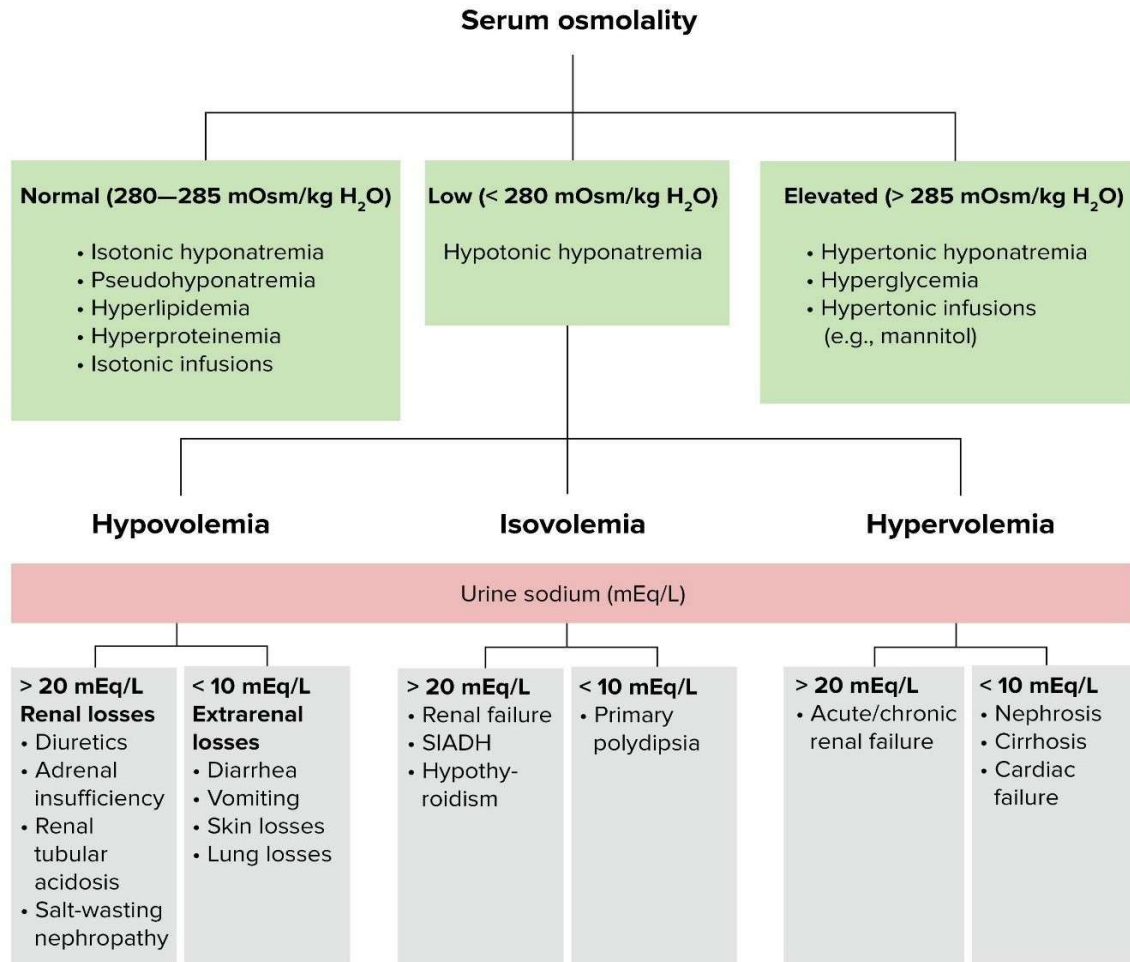
Hyperpituitarism (hyper secretion)	<p><u>Prolactinoma with hyperprolactinemia</u></p> <ul style="list-style-type: none"> ❖ Most common pituitary tumor (30% of pituitary tumors). ❖ Prolactinoma in women classically presents as galactorrhea, amenorrhea, and bone density due to suppression of estrogen. ❖ Prolactinoma in men classically presents as low libido and infertility. ❖ Treatment: dopamine agonists (e.g., bromocriptine.), transsphenoidal resection <p><u>Somatotropic adenoma with hypersecretion of growth hormone</u></p> <ul style="list-style-type: none"> ❖ This is the second most common pituitary tumor. ❖ Gigantism Results if adenoma develops before epiphyseal closure. ❖ Acromegaly Results if adenoma develops after epiphyseal closure, characterized by overgrowth of the jaws, face, hands, and feet, and generalized enlargement of viscera, along with hyperglycemia, osteoporosis, and hypertension. ○ Other results include local compression effects due to expansion of the tumor within the Sella turcica. ○ Treatment: Pituitary adenoma resection. If not cured, treat with octreotide (somatostatin analog) or pegvisomant (growth hormone receptor antagonist). dopamine agonists (e.g., cabergoline) <p><u>Corticotrophic adenoma and hypersecretion of adrenocorticotrophic hormone (ACTH)</u></p> <ul style="list-style-type: none"> ❖ Cushing disease <ul style="list-style-type: none"> ○ ↑ Production of adrenal cortical hormones due to a Corticotrophic adenoma of the pituitary. ❖ Cushing syndrome <ul style="list-style-type: none"> ○ ↑ Production of adrenal cortical hormones regardless of cause. ○ The cause may be ectopic ACTH production by various tumors (especially small cell carcinoma of the lung).
Hypopituitarism (Under secretion)	<ul style="list-style-type: none"> ❖ Nonsecreting pituitary adenoma, craniopharyngioma ❖ <u>Pituitary apoplexy:</u> <ul style="list-style-type: none"> ○ Sudden enlargement of pituitary tumour secondary to hemorrhage or infarction ○ Characterized by headache, vomiting, neck stiffness ❖ <u>Postpartum pituitary necrosis (Sheehan syndrome)</u> <ul style="list-style-type: none"> ○ It is caused by ischemic necrosis of the pituitary gland and is characteristically associated with hemorrhage and shock during childbirth. ○ Clinical manifestations are due at first to loss of gonadotropins, then to subsequent loss of thyroid-stimulating hormone (TSH) and ACTH. ❖ <u>Empty sella syndrome</u> <ul style="list-style-type: none"> ○ Atrophy or compression of pituitary (which lies in the sella turcica), often idiopathic, common in obese women. ❖ <u>Nelson syndrome</u> <ul style="list-style-type: none"> ○ Involves the development of large pituitary adenomas following bilateral adrenalectomy. ○ Presents with hyperpigmentation, headaches and bitemporal hemianopia. ○ It is one of the endocrine causes of hyperpigmentation

Posterior Pituitary (Neurohypophysis) Disorders

Syndrome Of Inappropriate ADH (SIADH) Secretion	<ul style="list-style-type: none">❖ SIADH is most commonly caused by ectopic production of ADH by various tumors, especially small cell carcinoma of the lung.<ul style="list-style-type: none">○ Clinical features:<ul style="list-style-type: none">○ Excessive free water retention→ Hyponatremia.○ Urine osmolality> serum osmolality○ Inability to dilute the urine.○ Cerebral edema○ Neurologic dysfunction❖ Mechanism:<ul style="list-style-type: none">○ ↑ADH, Excessive free water retention, Body responds to water retention with ↓aldosterone→ ↑ urinary Na+ secretion to normalize extracellular fluid volume Very low serum Na+ levels can lead to cerebral edema, seizures❖ Treatment:<ul style="list-style-type: none">○ Correction of hyponatremia must be done slowly to prevent osmotic demyelination syndrome (formerly known as central pontine myelinolysis).○ Fluid restriction○ Demeclocycline (reduces the responsiveness of the collecting tubule cells to ADH)												
Diabetes insipidus	<ul style="list-style-type: none">❖ Lack of ADH (central) or failure of response to circulating ADH (nephrogenic).❖ Clinical features: Polyuria, Intense thirst, and Inability to concentrate urine (dilute urine)❖ Classification <table><tr><th>Types</th><th>Central DI</th><th>Nephrogenic DI</th></tr><tr><td>Findings</td><td>❖ Lack of ADH</td><td>❖ Unresponsiveness of collecting tubules to ADH</td></tr><tr><td>Causes</td><td><ul style="list-style-type: none">❖ Pituitary tumor❖ Head trauma,❖ Inflammation or tumors of hypothalamus❖ DIDMOAD (or Wolfram's syndrome) is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Atrophy and Deafness</td><td><ul style="list-style-type: none">❖ Genetic❖ Electrolytes: ↑ Ca++, K+❖ Drugs: lithium, demeclocycline❖ (ADH antagonist), ofloxacin</td></tr><tr><td>Treatment</td><td><ul style="list-style-type: none">❖ Desmopressin acetate❖ Hydration</td><td><ul style="list-style-type: none">❖ Any underlying cause such as high blood calcium must be corrected to treat NDI.❖ The first line of treatment is hydrochlorothiazide and amiloride low-salt and low-protein diet</td></tr></table> <ul style="list-style-type: none">❖ <u>Water deprivation test:</u><ul style="list-style-type: none">○ Stage -1: (water deprivation for 0-8 hours):<ul style="list-style-type: none">▪ If after 8 hours, urine concentrates → primary polydipsia▪ If after 8 hours, urine does not concentrate→ DI (either CDI, NDI)○ Stage-2 (give desmopressin 2 ug IM)<ul style="list-style-type: none">▪ If urine concentrates after desmopressin → CDI▪ If urine does not concentrate after desmopressin→ NDI	Types	Central DI	Nephrogenic DI	Findings	❖ Lack of ADH	❖ Unresponsiveness of collecting tubules to ADH	Causes	<ul style="list-style-type: none">❖ Pituitary tumor❖ Head trauma,❖ Inflammation or tumors of hypothalamus❖ DIDMOAD (or Wolfram's syndrome) is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Atrophy and Deafness	<ul style="list-style-type: none">❖ Genetic❖ Electrolytes: ↑ Ca++, K+❖ Drugs: lithium, demeclocycline❖ (ADH antagonist), ofloxacin	Treatment	<ul style="list-style-type: none">❖ Desmopressin acetate❖ Hydration	<ul style="list-style-type: none">❖ Any underlying cause such as high blood calcium must be corrected to treat NDI.❖ The first line of treatment is hydrochlorothiazide and amiloride low-salt and low-protein diet
Types	Central DI	Nephrogenic DI											
Findings	❖ Lack of ADH	❖ Unresponsiveness of collecting tubules to ADH											
Causes	<ul style="list-style-type: none">❖ Pituitary tumor❖ Head trauma,❖ Inflammation or tumors of hypothalamus❖ DIDMOAD (or Wolfram's syndrome) is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Atrophy and Deafness	<ul style="list-style-type: none">❖ Genetic❖ Electrolytes: ↑ Ca++, K+❖ Drugs: lithium, demeclocycline❖ (ADH antagonist), ofloxacin											
Treatment	<ul style="list-style-type: none">❖ Desmopressin acetate❖ Hydration	<ul style="list-style-type: none">❖ Any underlying cause such as high blood calcium must be corrected to treat NDI.❖ The first line of treatment is hydrochlorothiazide and amiloride low-salt and low-protein diet											

Mnemonic: Diabetes insipidus → Deficient ADH (Central DI) or ADH Doesn't work (Nephrogenic DI), Dilute urine

- Serum osmolality of > 280 mOsm/kg → SIADH
- Serum osmolality of < 280 mOsm/kg → Water deprivation



THYROID GLAND

	Hyperthyroidism	Hypothyroidism
General	Weight loss despite ↑ appetite Heat intolerance	Weight gain despite appetite Cold intolerance
Skin	Sweaty, Pretibial myxedema	Dry skin, dry hairs
Heart	Systolic hypertension Tachycardia	Diastolic hypertension Bradycardia
Neurological	Anxiety, Hyperreflexia Irritability, Tremors	Carpal tunnel syndrome Delayed relaxation of reflexes
Reproductive	Oligomenorrhea, infertility	Menorrhagia, infertility
GIT	Diarrhea	Constipation
Eye	Exophthalmos (graves' disease)	
Labs	↑ T3 and T4, ↓ TSH	↓ T3 and T4, ↑ TSH

Causes	<ul style="list-style-type: none"> ❖ Graves' disease (toxic diffuse goiter) accounts for 50-60% of cases of Thyrotoxicosis. Toxic nodular goiter ❖ Toxic adenoma ❖ Subacute (De Quervain's) Thyroiditis ❖ Post-partum thyroiditis ❖ Amiodarone therapy 	<ul style="list-style-type: none"> ❖ Primary atrophic hypothyroidism: ❖ Most common cause ❖ Autoimmune disease, ❖ Hashimoto's thyroiditis: ❖ Autoimmune disease as above with goiter (positive microsomal antibodies) ❖ 10 times more common in women ❖ After thyroidectomy or radioiodine treatment ❖ Drug therapy (e.g. lithium, amiodarone, or anti- thyroid drugs such as carbimazole) ❖ Dietary iodine deficiency
Treatment	Carbimazole (SE: Agranulocytosis) Propylthiouracil, radioiodine and surgery	Levothyroxine (Side effect-- atrial fibrillation)

<u>Hyperthyroidism</u>	<p><u>Graves' disease</u></p> <ul style="list-style-type: none"> ❖ Most common cause of hyperthyroidism ❖ Associated with HLA-DR3 and HLA-B8. Type II hypersensitivity ❖ Thyroid-stimulating immunoglobulin (TSI), an IgG antibody, that binds to TSH receptors and mimics the action of TSH causing ↑ release of thyroid hormone ❖ A similar reaction with thyroid growth immunoglobulin (TGI) stimulates glandular hyperplasia and enlargement. ❖ Besides all other clinical signs and symptoms of hyperthyroidism there is Pretibial myxedema (infiltrative dermopathy) and Exophthalmos <p><u>Thyroid storm</u></p> <ul style="list-style-type: none"> ❖ Life-threatening condition, associated with untreated or undertreated hyperthyroidism. ❖ significantly worsens in the setting of acute stress such as infection, trauma, and surgery ❖ Presents with tachycardia (>140 bpm), agitation, restlessness, fever, diarrhea, coma, hyperthyroidism, and tachyarrhythmia (cause of death). ❖ Treatments (4 P's) <ul style="list-style-type: none"> ○ β-blockers (e.g., Propranolol), Propylthiouracil, Prednisolone, Potassium iodide (Lugol iodine) <p><u>Subacute (De Quervain's) thyroiditis</u></p> <ul style="list-style-type: none"> ❖ Thought to occur following viral infection and typically presents with hyperthyroidism, Painful goiter, Self-limiting. ❖ Treatment: <ul style="list-style-type: none"> ○ Steroids and propranolol ○ Carbimazole and PTU are ineffective (As inc hormones are due to destruction not due to inc production)
<u>Hypothyroidism</u>	<p>Hypothyroidism manifests as myxedema in adults or as Cretinism in Children</p> <p><u>Myxedema</u></p> <ul style="list-style-type: none"> ❖ Causes <ul style="list-style-type: none"> ○ Therapy for hyperthyroidism with surgery, irradiation, or drugs, which is a common cause of myxedema in the United States ○ Iodine deficiency ○ Hashimoto thyroiditis ▪ hypothyroidism + goiter + anti-TPO antibodies ▪ Most common cause of hypothyroidism in iodine-sufficient regions. ▪ Autoimmune disorder with antithyroid peroxidase (antimicrosomal) and antithyroglobulin antibodies. ▪ Associated with ↑ risk of non-Hodgkin lymphoma (B-cell origin). ▪ Histology: Hürthle cells, lymphoid aggregates with germinal centers

	Cretinism (Congenital hypothyroidism) <ul style="list-style-type: none"> ❖ Causes <ul style="list-style-type: none"> ○ Iodine deficiency ○ Maldevelopment of the thyroid gland ○ Failure of the fetal thyroid to descend from its origin at the base of the tongue ❖ Characteristics (6 P's) <ul style="list-style-type: none"> ○ Poor brain development (Severe mental retardation) ○ Protuberant tongue (Large tongue) ○ Protuberant abdomen, Protruding umbilicus (umbilical hernia) ○ Puffy-faced child
	Other Causes Of Hypothyroidism <ul style="list-style-type: none"> ❖ Goitrogens (eg., Amiodarone, lithium), ❖ Wolff-Chaikoff effect (thyroid gland down-regulation in response to iodide)

THYROID CANCER

Papillary carcinoma	<ul style="list-style-type: none"> ○ Most common thyroid cancer ○ Palpable lymph nodes (Lymphatic metastasis is common) ○ Post radiation in head and neck (One of the causes) ○ Excellent prognosis because it's slow growing ○ Histology: Popping eyes (Clear nuclei, Orphan Annie Eyes), Psammoma bodies
Follicular carcinoma	<ul style="list-style-type: none"> ❖ Blood borne metastasis, invades capsule ❖ Uniform Follicles. ❖ Diagnosis relies on the identification of capsular and/or lymphovascular invasion, because these tumors are in all other respects indistinguishable from follicular adenomas
Medullary Carcinoma (MEN-2)	<ul style="list-style-type: none"> ❖ Originates from C cells of the thyroid. ❖ It produces Calcitonin. a calcium-lowering hormone ❖ Associated with MEN 2A and 2B
Anaplastic carcinoma	<ul style="list-style-type: none"> ❖ Tends to occur in older patients and has a very poor prognosis

PARATHYROID GLAND

Hypoparathyroidism	<ul style="list-style-type: none"> ❖ It refers to ↓ PTH secretion → resulting in hypocalcaemia. ❖ Causes: <ul style="list-style-type: none"> ○ Accidental surgical excision during thyroidectomy (most common) ○ DiGeorge Syndrome (congenital Thymic hypoplasia) ❖ Manifestation: <ul style="list-style-type: none"> ○ Tetany (intermittent muscular spasms) <ul style="list-style-type: none"> ▪ Chvostek sign → tapping of facial nerve causes contraction of facial muscles. ▪ Trousseau sign → occlusion of brachial artery with BP cuff causes carpal spasm.
Pseudohypoparathyroidism	<ul style="list-style-type: none"> ❖ Also known as Albright hereditary osteodystrophy ❖ Autosomal dominant condition in which PTH production is normal, but the kidneys are unresponsive to PTH (end-organ resistance to PTH). Manifestations include: <ul style="list-style-type: none"> ○ Short stature ○ Short 4th and 5th metacarpals and metatarsals ○ Calcification of basal ganglia

Hyperparathyroidism

	Primary Hyperparathyroidism	Secondary hyperparathyroidism	Tertiary hyperparathyroidism
Causes	❖ Parathyroid adenoma (most common) ❖ Parathyroid carcinoma	Chronic renal failure Vitamin D deficiency	Refractory (autonomous) hyperparathyroidism resulting from chronic renal failure. Prolonged secondary hyperparathyroidism, in which continuous stimulation results in parathyroid adenoma and autonomous PTH secretion
Ca	↑	↓	↑
Po4	↓	↑	↑
PTH	↑	↑	↑
Features	Painful bones: fractures, osteoporosis, Osteitis fibrosa cystica Renal stones due to ↑ Ca ⁺⁺ Abdominal groans → constipation due to ↑ Ca ⁺⁺ Psychic moans → depression, seizures	Renal osteodystrophy	Renal osteodystrophy/ autonomous parathyroid adenoma

Osteitis fibrosa cystica

- ❖ A disorder resulting in a loss of bone mass, a weakening of the bones as their calcified supporting structures are replaced with fibrous tissue, and the formation of cyst-like brown tumors in and around the bone, causes bone pain. It is due to ↑PTH, classically associated with 1° (but also seen with 2°) hyperparathyroidism.

Renal osteodystrophy

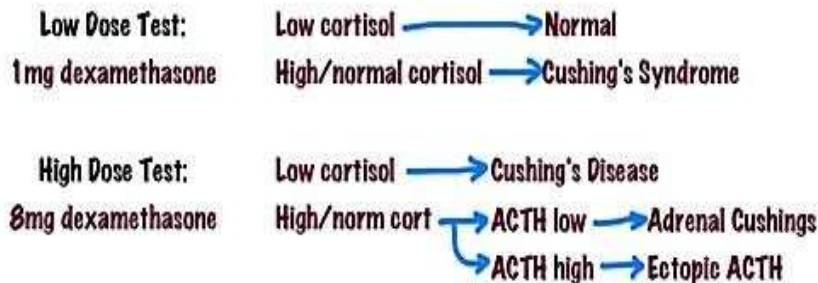
A bone disease that occurs when your kidneys fail to maintain proper levels of calcium and phosphorus in blood.

DISORDERS OF ADRENAL CORTEX**Cushing syndrome**

Causes	<ul style="list-style-type: none"> ❖ Exogenous: Exogenous corticosteroid medication (most common) ❖ Endogenous causes: <ul style="list-style-type: none"> ○ Cushing disease: ACTH-secreting pituitary adenoma (Most common endogenous) ○ Adrenal cortical adenoma or adrenal carcinoma ○ Ectopic production of ACTH → small cell carcinoma of the lung
Features	<ul style="list-style-type: none"> ❖ Non-specific → secondary diabetes, HTN, osteoporosis ❖ More specific → central obesity with extremity wasting, moon facies, buffalo hump. ❖ Most specific → spontaneous bruising, skin striae, proximal myopathy
Labs	○ Sodium ↑, Potassium ↓, Glucose ↑, Calcium ↓
Diagnosis	<p><u>Step-1: To know whether patient has Cushing syndrome.</u></p> <ul style="list-style-type: none"> ○ 24 hours urinary free cortisol ○ Dexamethasone suppression test <ul style="list-style-type: none"> ▪ Normal people suppress cortisol levels ▪ Cushing syndrome failure to suppress cortisol levels. <p><u>Step-2 To know cause of Cushing syndrome</u></p> <ul style="list-style-type: none"> ○ Measure Plasma ACTH level: <ul style="list-style-type: none"> ▪ ↓ACTH level → source is adrenal glands ▪ ↑ACTH level → source is either Pituitary ACTH tumor or Ectopic ACTH production. <p><u>Step-3 To differentiate between Pituitary and ectopic ACTH production</u></p> <ul style="list-style-type: none"> ○ 48-hour high dose dexamethasone suppression test: <ul style="list-style-type: none"> ▪ It involves administration of dexamethasone 6 hourly for 48 hours, measuring 24-hour urinary cortisol 2nd day. ▪ If ACTH is suppressed source is pituitary gland, next step is do MRI brain. ▪ If ACTH is not suppressed → source is ectopic ACTH, next step is do CT chest/abdomen

Dexamethasone Suppression Test

Given at night (10pm), measured in the morning (9am)



Hyperaldosteronism

Primary Hyperaldosteronism (Conn syndrome)	<ul style="list-style-type: none"> ❖ Cause is primary hyper production of adrenal mineralocorticoids. ❖ Clinical characteristics include hypertension, sodium and water retention, and hypokalemia. ❖ Decreased serum renin occurs due to negative feedback of increased blood pressure on renin secretion. Findings → inc aldosterone, low renin
Secondary Hyperaldosteronism	<ul style="list-style-type: none"> ❖ This condition is secondary to renal ischemia, renal tumors, and edema (e.g., cirrhosis, Nephrotic syndrome, cardiac failure). ❖ The cause is stimulation of the renin-angiotensin system. ❖ Renin synthesized in the juxtaglomerular apparatus of the kidney promotes the conversion of angiotensinogen to angiotensin I, which is converted catalytically by angiotensin-converting enzyme (mainly in the lung) to angiotensin II. ❖ The release of aldosterone is facilitated by angiotensin II. ❖ Findings: ↑ aldosterone, ↑ renin.

Adrenal Insufficiency

Primary Adrenal Insufficiency	<p><u>Addison's Disease</u></p> <ul style="list-style-type: none"> ❖ Causes: <ul style="list-style-type: none"> ○ This disorder is most commonly due to idiopathic adrenal atrophy. ○ It can also be caused by tuberculosis (formerly most common cause). ○ Metastatic tumor ○ Various infections. ❖ Characteristics <ul style="list-style-type: none"> ○ Hypotension (Postural hypotension) ○ Increased pigmentation of skin. ○ Serum Na, Cl⁻, glucose, and HCO₃⁻ → decreased ○ Serum potassium → increased ❖ Diagnosis: <ul style="list-style-type: none"> ○ Short synacthen test (short ACTH-suppression test): <ul style="list-style-type: none"> ▪ 250 pg ACTH IM injection given. ✚ Normal individual cortisol ✚ Primary adrenal insufficiency → ↑ ACTH ✚ Secondary adrenal insufficiency → ↓ ACTH <p><u>Waterhouse-Friderichsen Syndrome</u></p> <ul style="list-style-type: none"> ❖ This catastrophic adrenal insufficiency and vascular collapse is due to hemorrhagic necrosis of the adrenal cortex. ❖ This syndrome is associated with DIC and meningococcal meningitis characteristically due to meningococcaemia.
Secondary Adrenal Insufficiency	<ul style="list-style-type: none"> ❖ Seen with ↓ pituitary ACTH production. ❖ No skin/mucosal hyperpigmentation ❖ No hyperkalemia (aldosterone synthesis preserved due to intact renin angiotensin-aldosterone axis)

Tumors of the Adrenal Medulla

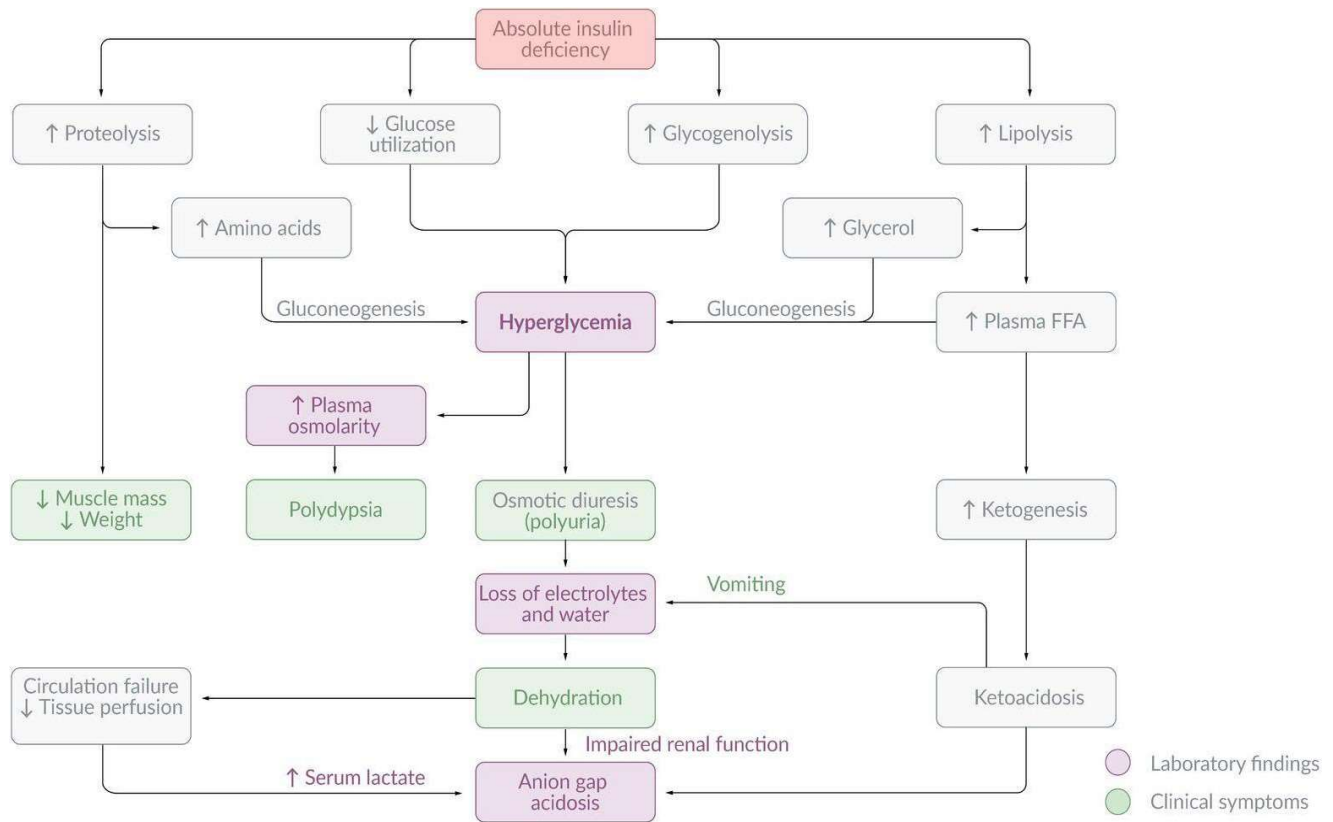
Pheochromocytoma (Paranglioma)	Causes	<ul style="list-style-type: none"> ❖ Most common tumor of the adrenal medulla in adults ❖ Derived from chromaffin cells (arise from neural crest). ❖ May be associated with MEN 2A, 2B, von Hippel-Lindau disease
	Rule of 10's	❖ 10% malignant 10% bilateral, 10% extra-adrenal (e.g., bladder wall), 10% calcify and 10% kids
	Symptoms	<ul style="list-style-type: none"> ❖ Episodic hyper adrenergic symptoms (5P's): <ul style="list-style-type: none"> ○ Pressure (↑BP), Pain (headache), Perspiration ○ Palpitations (tachycardia) and Pallor
	Lab	❖ Increased urinary excretion of catecholamines and their metabolites (metanephrine, normetanephrine, and vanillylmandelic acid) is characteristic.
	Treatment	Mnemonic: Phenoxybenzamine (16 letters) is given for Pheochromocytoma (also 16 letters). <ul style="list-style-type: none"> ❖ Irreversible α-antagonists (e.g., phenoxybenzamine) followed by B-blockers prior to tumor resection. ❖ α-blockade must be achieved before giving B-blockers to avoid a hypertensive crisis.
Neuroblastoma		❖ Most common tumor of the adrenal medulla in children. Usually, <4 years old
		❖ Abdominal distension and a firm, irregular mass that can cross the midline (while in Wilms tumor, which is renal cancer in children, it is smooth)
		❖ Less likely to develop hypertension than with pheochromocytoma.
		❖ Can also present with opsoclonus-myoclonus syndrome ("dancing eyes -dancing feet").
		❖ It is comprised of small round blue cells which form characteristic rosette-like structures
		❖ ("Homer Wright" pseudorosettes)
		❖ Urinary catecholamines and catecholamine metabolites in urine are the same as in pheochromocytoma
		❖ The tumor is characterized by amplification of the N- myc oncogene

Adrenal Virilism (Adrenogenital Syndrome or congenital adrenal hyperplasia-CAH)

Congenital enzyme defects → ↓ cortisol production and compensatory ↑ ACTH, with resultant adrenal hyperplasia with androgenic steroid production

Causes	<ul style="list-style-type: none"> ❖ 21-hydroxylase deficiency (most common) → salt retention and hypertension ❖ 11-hydroxylase deficiency → results in salt retention and hypertension
Characteristics	❖ Virilism in females and precocious puberty in males

DISORDERS OF ENDOCRINE PANCREAS

DIABETES MELLITUS

Clinical features: 3 Ps --- Polyuria, Polydipsia, polyphagia, Weight loss, blurred Vision

Diagnosis

Criteria-1	❖ Symptomatic patients plus Abnormal venous glucose on ONE occasion i.e. FBS ≥ 126 mg/dL (≥ 7 mmol/L) OR RBS ≥ 200 mg/dL (≥ 11 mmol/L)
Criteria-2	❖ Asymptomatic patients plus Abnormal venous glucose on TWO occasions i.e. FBS ≥ 126 mg/dL (≥ 7 mmol/L) OR RBS ≥ 200 mg/dL (≥ 11 mmol/L)
Criteria-3	❖ HbA1C $\geq 6.5\%$ Conditions where HbA1c may not be used for diagnosis: <ul style="list-style-type: none"> ○ Haemoglobinopathies and Hemolytic anemias ○ Untreated iron deficiency anemia ○ Suspected gestational diabetes. ○ Children, HIV or CKD To convert HbA1c into mmol/L = average plasma glucose = $(2 \times \text{HbA1c}) - 4.5$ To convert mmol/L into mg/dL = multiply it with 18

Diabetes UK guidelines

❖ Diabetes UK suggests people with IFG should then be offered an OGTT to rule out a diagnosis of diabetes, also used for gestational diabetes.

❖ OGTT

○ Preparation before test:

✓ Unrestricted carbohydrate diet for 3 days

✓ Overnight fasting for at least 8 hours

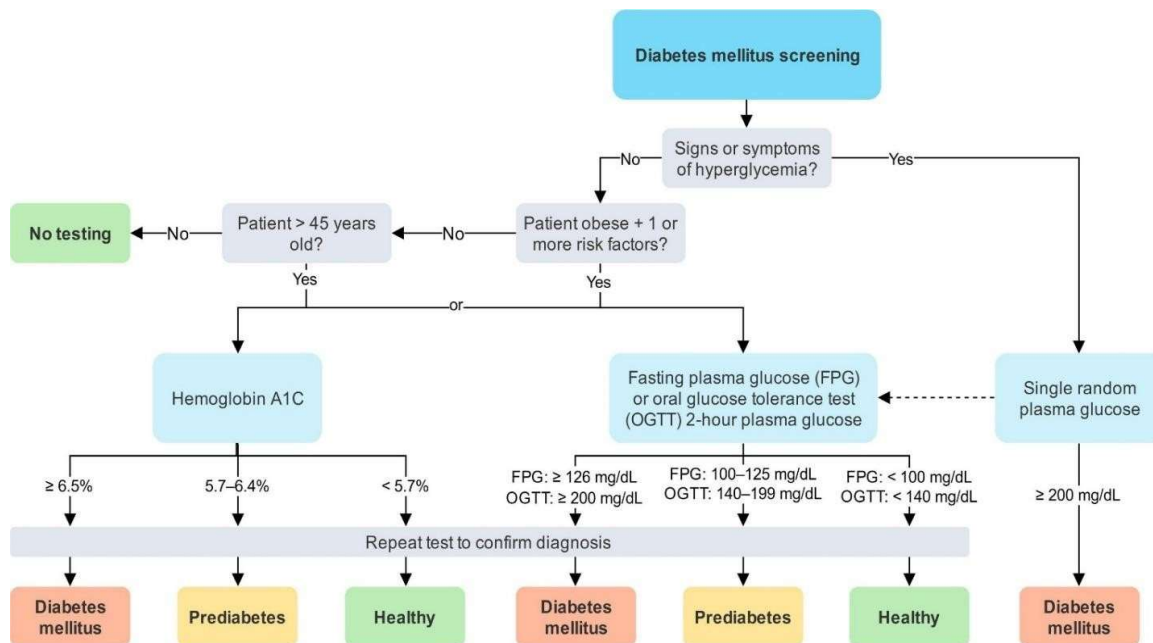
✓ Sampling: plasma glucose is measured before and 2 hours after 75g glucose drink

	Normal	Impaired Glucose tolerance	DM
Fasting	<7mmol/L (<126mg/dL)	<7mmol/L (<126mg/dL)	≥7mmol/L (≥126mg/dL)
2 hours after glucose	<7.8mmol/L (<140mg/dL)	7.8—11 mmol/L (140—199mg/dL)	≥11.1 mmol/L (≥200mg/dL)

❖ Management of Impaired glucose tolerance test:

○ lifestyle modification: weight loss, increased exercise, change in diet at least yearly follow-up with blood tests is recommended.

○ NICE recommend metformin for adults at high risk whose blood glucose measure (fasting plasma glucose or HbA1c 6.0-6.4) shows they are still progressing towards type 2 diabetes, despite their participation in an intensive lifestyle-change programme'

**Complications of Diabetes**

Acute complications: Hypoglycemia, Hyperosmolar hyperglycemic non-ketotic coma, diabetic ketoacidosis

Chronic complications: Microvascular and macrovascular complications

Microvascular → Retinopathy, nephropathy, neuropathy, diabetic foot, dermopathy

Macrovascular → CVS (IHD e.g., MI), Cerebrovascular (stroke), Peripheral vascular disease (e.g., critical limb ischemia)

- ❖ Hyperglycemia increases retinal blood flow and metabolism which leads to chronic retinal hypoxia stimulates production of growth factors causing new vessels formation and increased vascular permeability

❖ Classification:

Retinopathy Non-Proliferative

Mild NPDR	Moderate NPDR	Severe NPDR (4-2-1 rule)
1 or more microaneurysm	<ul style="list-style-type: none"> ○ Microaneurysm ○ Blot hemorrhages ○ Hard exudates ○ Cotton wool spots ○ Venous bleeding/intra-arterial microvascular abnormalities less severe than in severe NPDR 	<ul style="list-style-type: none"> ○ Blot hemorrhages and microaneurysm in 4 quadrants ○ venous beading in at least 2 quadrants ○ IRMA in at least 1 quadrant

Proliferative Retinopathy:

Retinal neovascularization - may lead to vitreous hemorrhage.

Fibrous tissue forming anterior to retinal disc

More common in Type I DM, 50% blind in 5 years

- ❖ Hard exudates, macular haemorrhage

❖ Rx: Photocoagulation

❖ Cataract

❖ All patient should be checked annually

❖ Albumin: Creatinine ratio (ACR) in early morning specimen

○ ACR >2.5 in male, > 3.5 in female = microalbuminuria

❖ Rx: ACE or ARBs

❖ Weakness. Wasting and paraesthesia, Carpal tunnel syndrome

❖ Treatment: amitriptyline, duloxetine, gabapentin or pregabalin

CLASSIFICATION

Types	Type-1 diabetes mellitus (IDDM)	Type-2 Diabetes mellitus (NIDDM)
	❖ Also known as insulin dependent diabetes mellitus (IDDM)	❖ Also known as non-insulin dependent diabetes mellitus (NIDDM)
Cause	❖ Autoimmune destruction of β cells	<ul style="list-style-type: none"> ❖ \uparrow resistance to insulin, ❖ progressive pancreatic β-cell failure
Epidemiology	<ul style="list-style-type: none"> ❖ Younger patients usually < 30 years ❖ Usually, lean 	<ul style="list-style-type: none"> ❖ Older patients usually > 30 years ❖ Usually, overweight
Genetics	<ul style="list-style-type: none"> ❖ Family history uncommon ❖ HLA DR3 and HLA DR4 association ❖ 30-50% concordance rate in identical in identical twins 	<ul style="list-style-type: none"> ❖ Family history common ❖ No HLA association ❖ >90% concordance rate in identical twins

Maturity-onset diabetes mellitus of the young (MODY)

- ❖ This autosomal dominant syndrome is characterized by mild hyperglycemia and hyposecretion of insulin but no loss of beta cells.
- ❖ It has an earlier onset (typical age < 25 years old) than type 2 diabetes mellitus.
- ❖ It is caused by a diverse group of single gene defects. Such as glucokinase gene (MODY 2), HNF-1 alpha gene (MODY 3 most common)

Secondary Diabetes Mellitus

Hereditary hemochromatosis	<ul style="list-style-type: none"> • Arthralgia, Bronze skin. Cardiomyopathy, Cirrhosis of liver. Diabetes (pancreatic damage). Hypogonadism (anterior pituitary damage) ❖ Bronze diabetes ❖ Characteristics include excess iron absorption and parenchymal deposition of hemosiderin, with reactive fibrosis in organs, especially the pancreas, liver, and heart
Pancreatic cancer	❖ Diabetes mellitus may be the presenting sign.

Cushing syndrome	❖ Produces hyperglycemia as a result of increased gluconeogenesis and impaired peripheral utilization of glucose
Acromegaly	❖ Produces hyperglycemia due to the anti-insulin like effect of growth hormone.
Pregnancy	❖ Pregnancy may be associated with transient diabetes mellitus (gestational diabetes). ❖ Diabetes mellitus is characteristically associated with increased fetal birth weight at increased fetal mortality, notably from neonatal respiratory distress syndrome (hyaline membrane disease).

Type 2 Diabetes Medications

*ROH = Risk of Hypoglycemia

Drug Class	Examples	Mechanism of Action	Side Effects	ROH*	Contraindications
Biguanides	Metformin	Increase insulin sensitivity; Decrease hepatic gluconeogenesis	Nausea, vomiting, diarrhea, vitamin B12 deficiency, lactic acidosis (rare)	No	CKD, heart disease, liver disease, metabolic acidosis
Thiazolidinediones	Pioglitazone	Increase insulin sensitivity; Decrease hepatic gluconeogenesis	Weight gain, fluid retention, heart failure, bladder cancer risk, fractures, increase HDL	No	Heart failure, osteoporosis, history of bladder cancer
Sulfonylureas	Glipizide	Stimulate insulin secretion by inhibiting/closing beta cell ATP-sensitive K ⁺ channels	Hypoglycemia, weight gain	Yes	CKD, hepatic impairment
SGLT-2 Inhibitors	Dapagliflozin	Decrease glucose reabsorption in the kidney; Increase glucose excretion	Weight loss, thirst, increased urination, UTI risk, AKI	No	Renal impairment
DPP-4 Inhibitors	Sitagliptin	Increase GLP-1, which increases insulin secretion	GI upset, headaches, URIs, joint pain, risk of pancreatitis	No	Pancreatitis, heart failure, angioedema, DKA
GLP-1 Mimetics	Exenatide	Increase insulin secretion; Inhibit glucagon secretion	Nausea, vomiting, diarrhea, pancreatitis, weight loss, AKI	No	Pancreatitis, CKD, medullary thyroid cancer, gastroparesis
Insulin	"Basal"	Exogenous insulin provided	Weight gain	Yes	Hypokalemic drugs, dose adjusted for renal/liver failure

Multiple Endocrine Neoplasia (MEN) Syndrome

MEN is inherited as an autosomal dominant.

MEN-I (Wermer syndrome)	MEN-II a (Gipple syndrome)	MEN-II b
<ul style="list-style-type: none"> ❖ 3p¹⁵ includes hyperplasia or tumors of the <ul style="list-style-type: none"> ○ pituitary ○ parathyroid. or ○ Pancreatic islets ❖ In addition, it may include hyperplasia or tumors of the thyroid or adrenal cortex. 	<ul style="list-style-type: none"> ❖ Medullary thyroid cancer (70%) ❖ 2P's <ul style="list-style-type: none"> ○ Pheochromocytoma ○ Parathyroid (60%) 	<ul style="list-style-type: none"> ❖ Medullary carcinoma ❖ Multiple mucocutaneous neuromas or ganglioneuromas. ❖ 1P's <ul style="list-style-type: none"> ○ pheochromocytoma,
It is linked to mutations in the MEN/ gene	❖ It is linked to mutations in RET oncogene	❖ It is linked to mutations in RET oncogene
Most common presentation = hypercalcemia	❖ Note: when a diagnosis of pheochromocytoma is made, the finding of characteristic RET mutations would justify prophylactic thyroidectomy (because of the danger of fatal medullary carcinoma of the thyroid).	<ul style="list-style-type: none"> ❖ In contrast to MEN IIa, it does not induce hyperparathyroidism. ❖ It is linked to different mutations in the ret oncogene compared with MEN IIa.

Neuroendocrine Tumors

- ❖ Heterogeneous group of neoplasms originating from neuroendocrine cells (which has traits like nerve cells and hormone-producing cells)

Carcinoid syndrome	<ul style="list-style-type: none"> ❖ Neuroendocrine tumors When metastatic to the liver, can lead to carcinoid syndrome. ❖ Caused by the elaboration of vasoactive peptides and amines, especially serotonin. ❖ <u>clinically presentation:</u> <ul style="list-style-type: none"> ○ Cutaneous flushing Watery diarrhea and abdominal cramps and Bronchospasm. ○ Valvular lesions of the right side of the heart ▪ Carcinoid tumors most commonly arise in small intestine and lung.
Insulinoma	<ul style="list-style-type: none"> ❖ Tumor of pancreatic β cells characterized by overproduction of insulin leading to hypoglycemia. ❖ <u>Clinical characteristics include the Whipple triad:</u> <ul style="list-style-type: none"> ❖ Episodic hyperinsulinemia and hypoglycemia. ❖ Central nervous system (CNS) dysfunction temporally related to hypoglycemia (confusion, anxiety, stupor, convulsions, coma) ❖ Dramatic reversal of CNS abnormalities by glucose administration <u>To differentiate between endogenous insulin production from exogenous insulin</u> ❖ Circulating C-peptide is characteristically increased in patients with insulinoma. ❖ In contrast. C-peptide is not increased by exogenous insulin administration because it is removed during the purification of commercial insulin preparations. ❖ Treatment -- Surgical resection.
Glucagonoma	<ul style="list-style-type: none"> ❖ Tumor of pancreatic alpha cells resulting in overproduction of glucagon causing secondary diabetes mellitus ❖ <u>Clinical features-Mnemonic 5D's</u> ❖ Dermatitis (necrolytic migratory erythema), Diabetes (Hyperglycemia), ❖ DVT, Declining weight, Depression. Treatment: ❖ Octreotide & surgery
Gastrinoma	<ul style="list-style-type: none"> ❖ This tumor is often malignant and sometimes occurs in extrapancreatic sites. ❖ It results in gastrin hypersecretion and hypergastrinemia. ❖ It is associated with the Zollinger-Ellison syndrome (marked gastric hypersecretion of hydrochloric acid, recurrent peptic ulcer disease, and hypergastrinemia)
VIPoma	<ul style="list-style-type: none"> ❖ A rare tumor marked by secretion of vasoactive intestinal peptide (VIP). ❖ It is associated with Watery Diarrhea, Hypokalemia, and Achlorhydria ❖ WDHA) syndrome, (Also known as Verner-Morrison syndrome or pancreatic cholera.

PAST PAPERS BCQs

1. **Adenohypophysis** receives input from hypothalamic- hypophyseal portal **system**
2. **Neurohypophysis** receives input from hypothalamic-hypophyseal **tract**
3. Hormones secreted from hypothalamus to posterior pituitary are stored in nerve endings
4. ADH and oxytocin are neurosecretory hormones
5. Infundibular stalk is surrounded by pars tuberalis
6. cGMP is used as 2nd messenger by ANP, BNP, NO
7. prolactin inhibition factor is dopamine
8. Key stress hormone is cortisol. Earliest to be released in stress is CRH followed by ACTH
9. Hormone released in stress that causes vasoconstriction also is norepinephrine (catecholamines)
10. Most common enzyme deficiency in steroid hormone biosynthesis is of 21 alpha hydroxylase deficiency
11. ADH released from supraoptic nuclei. Oxytocin from paraventricular nuclei
12. Free calcium binds with albumin in serum.
13. At the end of marathon, athlete will have high glucagon and low insulin
14. Prolactinoma is the most common pituitary adenoma, causes amenorrhea, galactorrhea, loss of libido. In Microprolactinoma → levels b/w 1000-5000. In Macroprolactinoma → > 5000 prolactin levels
15. Specific test for Growth hormone deficiency is Insulin stimulation test
16. Growth hormones exert its effect by IGF-1 or somatomedins C
17. PTH causes demineralization of bone. Remineralization done by vit D
18. Lactational amenorrhea is due to inc prolactin
19. Insulin increases activity of lipoprotein lipase
20. Gluconeogenesis is the main function of cortisol
21. Thyroid hormones are anabolic to protein synthesis
22. Receptors for growth hormone (JAK-STAT pathway) tyrosine kinase receptor on plasma membrane
23. Hormone causing extrahepatic protein catabolism and anabolic to liver is Cortisol
24. Precursor of steroid hormones is cholesterol (read flow chart of synthesis of steroid hormones)
25. Potent stimulator of aldosterone is Hyperkalemia and hyponatremia. Prefer, serum K+
26. Insulin is anti-ketotic, while, glucagon is ketogenic. Immediate action of insulin is potassium entry inside cells. Action of insulin at cellular level is entry of glucose inside cells
27. Half life of insulin is 5 min, in fetus insulin inc in 3rd month. Low insulin causes ketogenesis
28. Growth hormone is stimulated by hypoglycemia > exercise > sleep (NREM)
29. Glucagon causes glycogenolysis, ketogenesis and gluconeogenesis
30. Secretin inc the release of insulin
31. HTN, headache, palpitations in 25 year old male most likely endocrine cause is Pheochromocytoma
32. 8 year old girl c/o hirsutism, enlarged genitalia and deepened voice. The likely cause is CAH. Deficiency of 21 a hydroxylase. Lab test to be done = 17 Hydroxyprogesterone
33. CCK inc the release of insulin and glucagon
34. Circadian rhythm is controlled by hormonal levels (i.e melatonin)
35. Excessive growth hormone after adolescence is called acromegaly
36. Somatostatin and histamine has paracrine effect (released at one site act locally in that area)
37. Leptin hormone released by adipocyte exert relation between weight and puberty
38. 25 hydroxylation of vit D occurs in liver 1 alpha hydroxylation occurs in kidney
39. Bone and cartilage growth is caused by growth hormone
40. For uncoupling of oxidative phosphorylation - main role played by Nor-epinephrine > thyroxine
41. Test to do for hypothyroidism = TSH, free T4, T3. TSH is more specific
42. Iodide oxidation occurs in follicular cells of thyroid. Thyroglobulin is produced by follicular cells
43. TSH is metabolized in liver by demethylation while, T3, T4 metabolized by De-iodination in liver
44. Vit D is regulated by serum Calcium levels
45. Strenuous exercise may cause hyperkalemia
46. Aldosterone maintains water and electrolyte balance. ADH regulated plasma or ECF volume
47. Veins of anterior pituitary contain highest ACTH in stress
48. Milk production is by Prolactin, oxytocin, cortisol. Milk let down / ejection by oxytocin
49. Immunostimulatory hormones: GH, thyroid hormones. Immunosuppression via steroids
50. Inc Angiotensin II inhibits renin but AT II stimulates thirst

51. Potent stimulator of renin is Sympathetic stimulation via renal nerves > hypos (low Na, Low K)
52. Nausea is the most potent stimulator of ADH release. Prefer, nausea > inc serum osmolarity
53. 5% dextrose will cause ADH inhibition. Because it is hypotonic – raises ECF volume → ADH inhibition
54. Cortisol increase neutrophils but decrease lymphocytes and eosinophils
55. In Addison's disease (low adrenal steroids) – Raised lymphocytes, eosinophils, but low neutrophils
56. Maximum β cells are present in tail of pancreas
57. A Labor is sweating while working in hot environment, it will help release of = ADH
58. Zona fasciculata is regulated by ACTH. Zone glomerulosa regulated by serum K⁺ levels
59. ACTH controls mainly cortisol release and to lesser extent adrenal androgens
60. Maximum concentration of Thyroid hormone in circulation is of T₄ (enter circulation in T₄ form)
61. Active form of thyroid hormone is T₃ (T₃ also required for fetal brain maturation, not thyroxine)
62. Hypothyroidism, Hyperthyroidism and Cushing syndrome are three common non-neurological causes of proximal muscle weakness. Serum Creatine Kinase is important to differentiate between these three i.e Proximal muscle weakness + Elevated CK = Hypothyroidism
Proximal muscle weakness + Normal CK = Hyperthyroidism and Cushing syndrome
63. A lady with history of PPH later was found to have decreased serum ACTH. What is the most likely cause = Atrophy of adrenal cortex (due to hemorrhage and ischemia)
64. Small cell cancer causes cushing syndrome (not cushing disease)
65. A lady presents with round face, fat on neck and abdomen, hirsutism and raised ACTH. what is the diagnosis? cushing disease
66. Pigmentation with high ACTH in cushing disease, while, No pigmentation + low ACTH in cushing syndrome
67. Old lady with cushing syndrome most imp symptom : Proximal myopathy > Abdominal striae
68. Female presents with hypertension and increasing weight. Which features would be most suggestive of Cushing's syndrome rather than simple obesity? Proximal myopathy > abdominal striae
69. In cushing syndrome pt develop abdominal striae due to Dec fibroblast activity
70. What is the most common cause of endogenous Cushing's syndrome? Small cell carcinoma of the lung
Remember: Cushing disease: - increased ACTH from pituitary that stimulates adrenal.
71. Cushing syndrome: - excess steroids due to any cause e.g iatrogenic or exogenous steroids most commonly.
72. Cushing triad: - headache, vomiting and papilledema.
73. Cushing reflex:- increased BP with reflex bradycardia.
74. Cushing ulcer:- peptic ulcer due to CNS trauma or tumor
75. Initial or accurate screening test for cushing syndrome is 24 hour Urinary cortisol levels
76. Test to confirm the cause of cushing syndrome is Dexamethasone suppression test
77. Most common cause of Addison disease is Tb (third world countries) and autoimmune (developed countries)
78. Meningococcal sepsis may cause acute adrenal crisis (salt craving > sugar craving)

Main types of insulin preparations				
Type	Onset	Peak	Duration	Comments
Rapid-acting insulin analogue	5-15 min	30-60 min	2-5 hr	Can be injected at the start of a meal
Short-acting (soluble/regular insulin)	30 min	1-3 hr	4-8 hr	Usually injected 15-30 minutes before a meal. Clear solution
Intermediate or long-acting insulin (isophane or zinc insulin)	1-2 hr (NPH, Lente)	4-8 hr	8-12 hr (NPH)	Used to control glucose levels between meals. May be combined with short-acting insulin
	2-3 hr (Ultralente)	4-8 hr	8-24 hr (Ultralente)	
Long-acting insulin analogue	30-60 min	No peak	16-24 hr	Usually taken once daily

RENAL & BODY FLUIDS

Functions of Kidney (A WET BED)

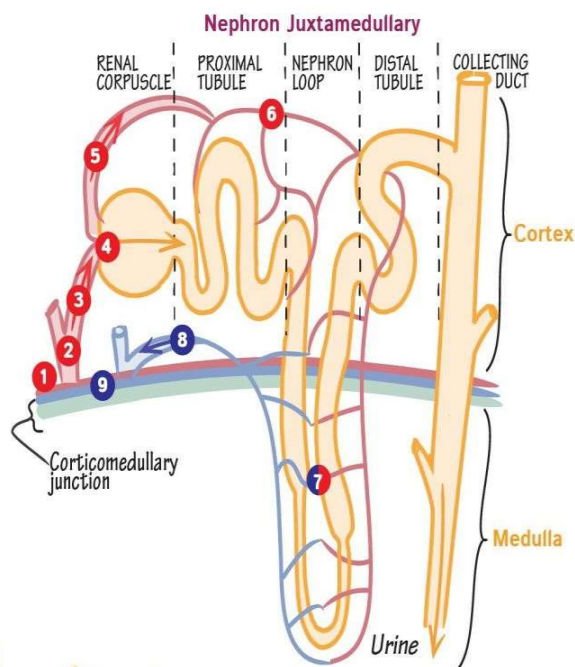
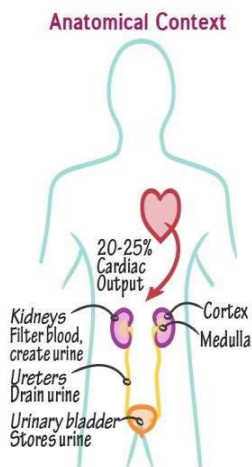
- A - controlling ACID-base balance.
- W - controlling WATER balance.
- E - maintaining ELECTROLYTE balance.
- T - removing TOXINS and waste products from the body.
- B - controlling BLOOD PRESSURE.
- E - producing the hormone ERYTHROPOIETIN.
- D - activating vitamin D.

Nephron is the structural and functional unit of kidney

RENAL OVERVIEW

+ Kidneys

- ✓ Regulate extracellular fluid osmolarity and volume.
 - ✓ Direct effects on blood volume, pressure, and acid/base balance.
- ✓ Efficiently filter blood to excrete wastes, including:
 - Toxins
 - Excess solutes and water
- ✓ Key roles in
 - ✓ Production of
 - Renin
 - Erythropoietin
 - Glucose
 - ✓ Activation of
 - Vitamin D
- ✓ Achieve these objectives via intrarenal mechanisms and input from the nervous and endocrine systems.



Nephron Types

Cortical (80%) —
Reside primarily in cortex.

Juxtamedullary (20%) —
Reside in both cortex and medulla; long nephron loop with vasa recta.

Blood Flow

- | | | |
|-----------------------|-----------------------------|---------------------|
| 1 Arcuate artery | 4 Glomerulus (of corpuscle) | 7 Vasa recta |
| 2 Interlobular artery | 5 Efferent arteriole | 8 Interlobular vein |
| 3 Afferent arteriole | 6 Peritubular capillaries | 9 Arcuate vein |

Extracellular fluid

- ❖ 1/3 of total body water.
- ❖ Present in spaces outside the cell
- ❖ Contains nutrients and ions essential for cell life that is why also called as internal environment of body.
- ❖ Major cations (positive charged ions): Na⁺
- ❖ Major anions (negative charged ions): Cl⁻ and HCO⁻
- ❖ ECF is Further divided into:
 - **Plasma:**
 - 1/4th of ECE

Intracellular Fluid

- ❖ 2/3rd of total body water
- ❖ It contains large amounts of potassium, magnesium, and phosphate ions.
- ❖ Major cations: K⁺ and Na⁺
- ❖ Major anions: proteins.

Mnemonic: HIKIN (High K Inside)

- Part of ECF present in blood contains plasma proteins.
- **Interstitial fluid:**
- 3/4th of ECF
- Part of ECF present in space between cells.
- contains little protein as compared to plasma ultra-filtrate of plasma

“60-40-20” rule

- TBW is 60% of body weight, ICF is 40% of body weight., ECF is 20% of body weight.
- So, Total body water in liters in a 70kg person is $\rightarrow 70 \times 0.6 = 42 \text{ L}$
- ICF in liters in a 70kg person is $\rightarrow 70 \times 0.4 = 28 \text{ L}$
- ECF in liters in a 70kg person is $\rightarrow 70 \times 0.2 = 14 \text{ L}$

Measuring the Volumes of the Fluid Compartments

Compartment	Marker used to measure volume	Major Cations	Major Anions
Total body water	Titrated H ₂ O, D ₂ O, Antipyrine		
ECF	Sulfate, Inulin, Mannitol	Na ⁺	Cl ⁻ , HCO ₃
Plasma (1/4 of ECF)	RISA (radio-iodinated serum albumin) Evans blue	Na ⁺	Cl ⁻ HCO ₃ - Plasma protein
Interstitial (% of ECF)	ECF minus plasma volume	Na ⁺	Cl ⁻ HCO ₃ -
ICF	TBW minus ECF	K ⁺	Organic phosphates protein

Shifts of Water between Compartments

- ❖ Osmosis is the flow of water from low solute to high solute concentration solution
- ❖ Osmolarity is concentration of solute particles.
- ❖ Plasma osmolarity (P_{osm}) is estimated as ; $P_{osm} = 2 \times Na^+ + Glucose/18 + BUN/2.8$
- ❖ At steady state, ECF osmolarity and ICF osmolarity are equal.
- ❖ To achieve this equality, water shifts between the ECF and ICF compartments.
- ❖ It is assumed that solutes such as NaCl and Mannitol do not cross cell membranes and are confined to ECF

Examples of Shift of Fluid between Compartments

Fluid Type	ECF Volume	ECF Osmolarity	Shift of Water and Results on ICF & ECF	Plasma Protein Concentration and Hematocrit
Infusion of Isotonic fluid e.g., 0.9% NS	↑	No change as the fluid is isotonic	No change in osmolarity, no shift of water b/w ICF and ECF	ECF volume ↑ So, it dilutes protein and RBCs. ↓ plasma protein, (↓ hematocrit)
Diarrhea (loss of isotonic fluid)	↓	No change as the fluid is isotonic	As no change in osmolarity, no shift of water b/w ICF and ECF	ECF volume ↓ So, it concentrates protein & RBCs. ↑ plasma protein + hematocrit
Excessive NaCl intake		↑ ECF osmolarity	Water shifts from ICF to ECF (because water molecules move from low solute to high solute concentration) as a result ↑ECF, ↓ICF	ECF vol. ↑ it dilutes protein and RBCs. ↓ plasma protein, ↓ hematocrit
Sweating in desert (more water is lost than salt)	↓	↑, because more water is lost than salt, so osmoles concentration is high comparatively	Water shifts out of cell ICF to ECF (because water molecules move from low solute to high solute concentration) as a result, ↑ECF, ↓ICF	ECF volume ↓ ↑ plasma protein, but hematocrit unchanged Because water shifts out of the RBCs, decreasing their volume and offsetting the concentrating effect of the decreased ECF volume
SIADH (gain of water)	↑ water retention	↓	Water shifts inside cell from ECF to ICF	ECF volume ↑ ↓ Plasma protein concentration But hematocrit unchanged

Because water shifts into RBCs, increasing their volume and offsetting the diluting effect of the gain of ECF volume

Renal Clearance

Indicates the volume of plasma cleared of a substance per unit time.

- ❖ The units of clearance are mL/min or mL/24 hour.
- $C = UV/P$ (mnemonic: UV light shining on Pee)
- where:
 - C = clearance (mL/min or mL/24 hour)
 - U = urine concentration (mg/mL)
 - V = urine volume/time (mL/min)
 - P = plasma concentration (mg / mL)

RENAL CLEARANCE

+ Key Concepts

- ✓ **Renal blood flow** —
Volume of blood that flows through the kidneys per minute (mL/min).
- ✓ **Renal plasma flow** —
Volume of blood plasma that flows through the kidneys per minute (mL/min).
- ✓ **Renal clearance** —
Volume of plasma that is completely removed of a given substance (mL/min).

+ Renal Blood Flow vs. Renal Plasma Flow

$$\text{Renal Blood Flow} = \frac{\text{Renal Plasma Flow}}{1 - \text{Hematocrit}}$$

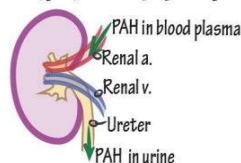
- ✓ RBF = 1000-1250 mL/min.
- ✓ RPF = 550-690 mL/min.

Renal Blood Flow (RBF)

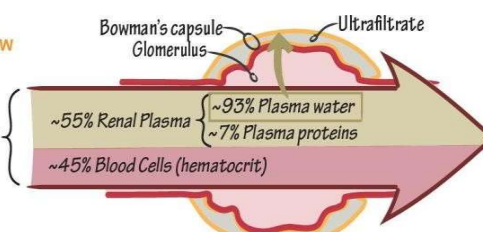
+ Renal Clearance

- ✓ Indicates whether a substance is filtered, reabsorbed, and/or secreted.
- ✓ **Fick Principle** —
Amount of a substance that enters the kidney is equal to the amount of substance that leaves it.

$$[\text{Renal artery}] = [\text{Renal vein}] + [\text{Ureter}]$$



- ✓ Renal clearance varies 0% to ~100%
 - Albumin = 0% (excluded from ultrafiltrate)
 - Glucose = 0% (completely reabsorbed)
 - PAH = ~100% (filtered and secreted)
 - Inulin = GFR (filtered, not reabsorbed or secreted)
- § Creatinine = ~GFR (filtered, minimally secreted)



+ Renal Clearance, Plasma Flow, and Blood Flow

$$\text{Clearance of PAH} = eRPF = \frac{[U]_{PAH} \cdot \dot{V}}{[P]_{PAH}}$$

📅 Clinical Example

- **Lab Results:**
 Urine concentration PAH = 550 mg/100 mL
 Urine flow rate = 1 mL/min
 Plasma concentration PAH = 1 mg/100 mL
 Hematocrit = 0.45

$$C_{PAH} = eRPF = \frac{550 \text{ mg/100 mL} \cdot 1 \text{ mL/min}}{1 \text{ mg/100 mL}} = 550 \text{ mL/min}$$

$$RBF = \frac{550 \text{ mL/min}}{1 - 0.45} = 1000 \text{ mL/min}$$

§ Clinical Correlation

- ✓ **GFR marker** —
 - A substance with a clearance equal to GFR;
 - Its clearance can be clinically determined to evaluate GFR and kidney functioning.
 - Creatinine is preferred because it is endogenous.

Renal Blood Flow

↓ RBF	Sympathetic nervous system and angiotensin II causing vasoconstriction
↑ RBF	Prostaglandins E2 and 12, bradykinin, nitric oxide, and dopamine causing vasodilation

Autoregulation of RBE

- ❖ RBF remains constant from 80 to 200 mm Hg by changing renal vascular resistance.
- ❖ **Mechanisms:**
 1. **Myogenic mechanism**
 ↑ renal arterial pressure → ↑ stretch → renal afferent arterioles contract in response to stretch increasing resistance to maintain constant blood flow.

2. Tubuloglomerular feedback

↑ renal arterial pressure → ↑ fluid to macula densa which causes constriction of afferent arterioles increasing resistance to maintain constant blood flow.

Measurement of Renal Plasma Flow (RPF)

- ❖ Renal plasma flow (RPF) can be estimated using para-aminohippuric acid (PAH) clearance.
- ❖ Between filtration and secretion, there is nearly 100% excretion of all PAH that enters the kidney.

$$RPF = C_{PAH} U_{PAH} \times V / P_{PAH}$$

- Where:
 - RPF renal plasma flow (mL/min or mL/24 hour)
 - C_{PAH} clearance of PAH (mL/min or mL/24 hour)
 - $[U]_{PAH}$ urine concentration of PAH (mg/mL)
 - V = urine flow rate (mL/min or mL/24 hour)
 - $[P]_{PAH}$ plasma concentration of PAH (mg/mL)

Glomerular Filtration Rate

- ❖ Inulin clearance can be used to calculate GFR.
- ❖ Because it is freely filtered and is neither reabsorbed nor secreted

$$GFR = C_{inulin} U_{inulin} \times V / P_{inulin}$$

where:

- GFR glomerular filtration rate (mL/min or mL/24 hour)
- $[U]_{inulin}$ urine concentration of inulin (mg/mL)
- V = urine flow rate (mL/min or mL/24 hour)
- $[P]_{inulin}$ = plasma concentration of inulin (mg/mL)

Determination of GFR

- ❖ GFR decreases Both BUN and serum creatinine increase.
- ❖ GFR decreases with age, although serum creatinine remains constant because of decreased muscle mass.

Starling Forces

- ❖ GFR can be expressed by the Starling equation as

$$GFR = K_f [(P_{GC} - P_{BS}) - (GC - \pi_{BS})]$$

Where

GFR is filtration across the glomerular capillaries (Normal GFR = 100 mL/min)

K_f is the filtration coefficient) of the glomerular capillaries. Normally, negative charges line the glomerular capillaries → restrict filtration of plasma proteins, which are also negatively charged

P_{GC} is glomerular capillary hydrostatic pressure

↑ by dilation of the afferent arteriole or constriction of the efferent arteriole (e.g. angiotensin II)

↑ in P_{GC} cause → ↑ net ultrafiltration pressure and GFR

P_{BS} is Bowman space hydrostatic pressure, ↑ by constriction of the ureters

↑ in P_{BS} cause → ↓ in net ultrafiltration pressure and GFR

π_{GC} is glomerular capillary oncotic pressure. Increased by increases in protein concentration

inc π_{GC} cause decreases in net ultrafiltration pressure and GFR.

Normally increases along the length of the glomerular capillary because filtration of water increases the protein concentration of glomerular capillary blood.

π_{BS} is Bowman Space oncotic pressure

❖ In short

- ↑ P_{GC} (Capillary hydrostatic pressure) → ↑ GFR
- ↑ P_{BS} (Bowman space hydrostatic pressure) → ↓ GFR
- ↑ π_{GC} (Capillary oncotic pressure) → ↓ GFR
- Afferent arteriole constriction → ↓ GFR, while, Efferent arteriole constriction inc GFR
- ↑ Plasma protein concentration → inc GFR

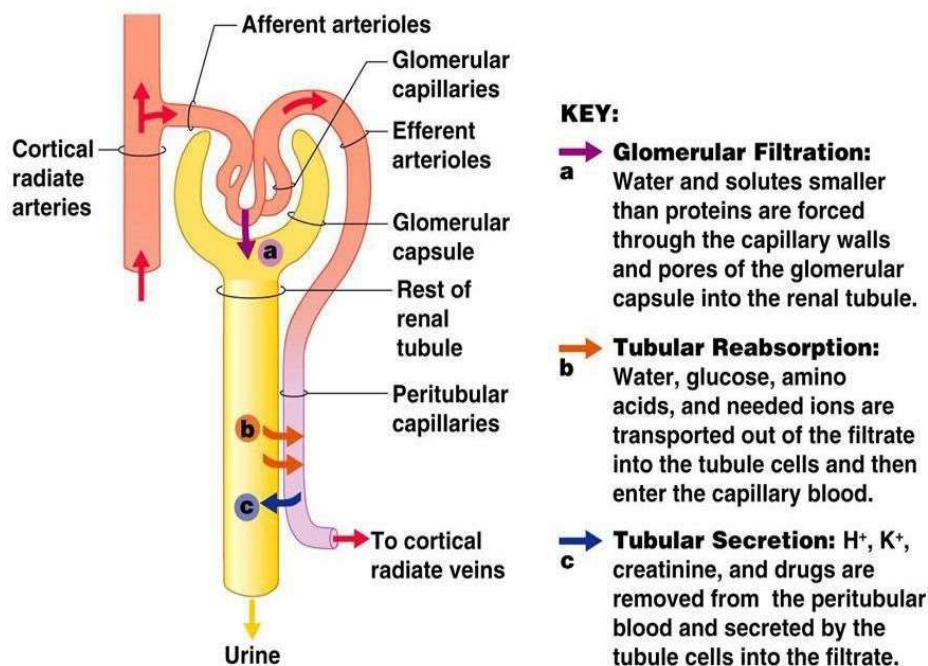
Reabsorption and Secretion

Calculation

- Filtered load = $GFR \times \text{plasma}$
- Excretion rates = $V \times \text{urine vol}$
- Reabsorption rate = Filtered load - Excretion rate
- Secretion rate = Excretion rate - Filtered load
- ❖ Filtered load > excretion rate → net reabsorption of the substance occurred.
- ❖ Filtered load < excretion rate → net secretion of the substance occurred.

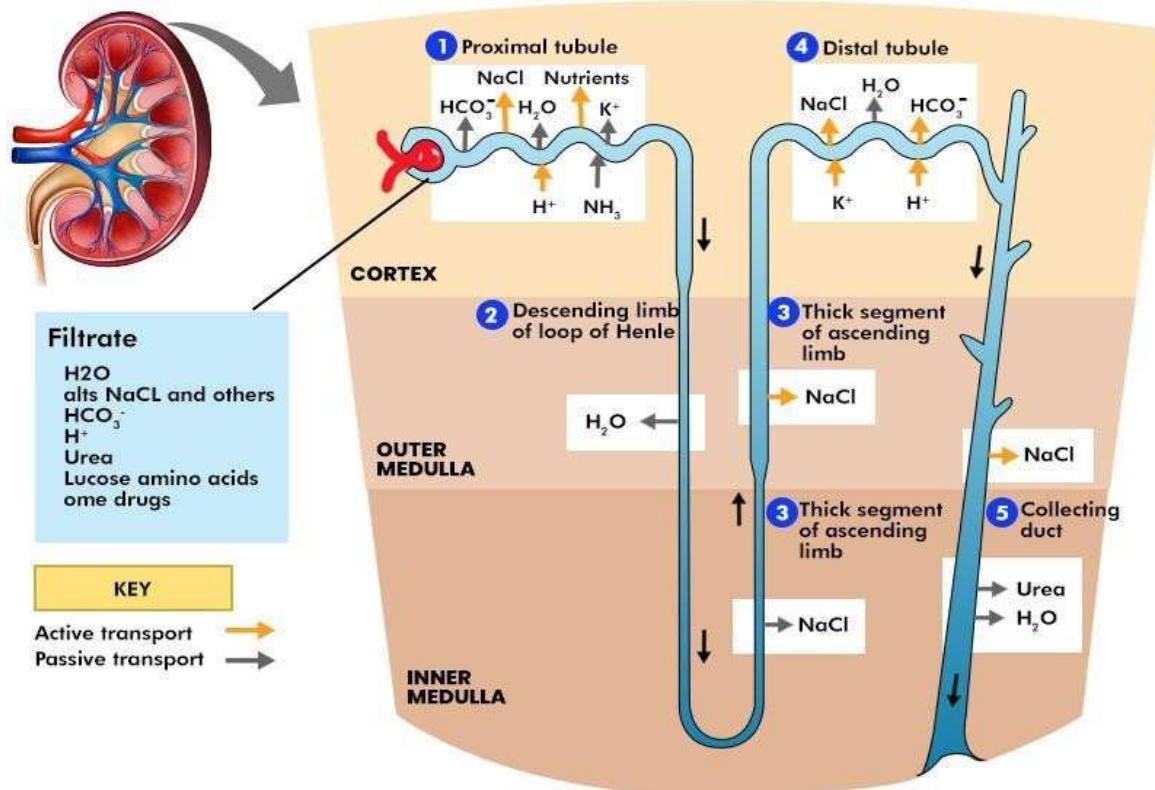
Reabsorption and Secretion of Different Substances / Markers

Glucose	<p>Reabsorption of glucose by Nat-glucose cotransport in the PCT</p> <p>Plasma glucose concentrations 200 → all of the filtered glucose can be reabsorbed.</p> <p>Plasma glucose concentrations > 375 more the carriers are saturated called T_m (transport maximum) → so no further reabsorption occurs.</p> <p>Excretion of glucose</p> <p>Plasma glucose concentrations < 200 mg/dL → all of the filtered glucose can be reabsorbed, so excretion is zero.</p> <p>Plasma glucose concentrations > 375 mg/dL, the carriers are saturated called T_m → so no reabsorption so if the plasma concentration increases, the additional filtered glucose cannot be reabsorbed and is excreted in the urine</p> <p>Threshold Defined as the plasma concentration at which glucose first appears in the urine is approximately 200 mg/dL.</p> <p>Splay is the region of substance clearance between threshold and T_m due to the heterogeneity of nephrons.</p> <p>NOTE:</p> <p>Normal pregnancy may decrease ability of PCT to reabsorb glucose and Amino acids, leading to glycosuria and aminoaciduria,</p>
Clearances of Substances	<p>PAH > K (high- K⁺ diet) > Inulin > Urea > Na⁺ > Glucose. Amino acids and HCO₃</p>



Renal Regulation of NaCl, K⁺, Urea, PO₄, Ca²⁺, Mg²⁺

	PCT	Loop of Henle	DCT & Collecting Duct	Effect of Hormone/ Drug
NaCl	<p>Early PCT:</p> <ul style="list-style-type: none"> Absorbs 67% of Na⁺ and H₂O by cotransport with glucose, amino acids, phosphate, and lactate <p>Na⁺ is also reabsorbed by counter transport via Na⁺-H⁺ exchange causing reabsorption of HCO₃</p> <p>Late PCT</p> <ul style="list-style-type: none"> Na⁺-Cl cotransporter. <p>Site Of Glomerulotubular Balance</p> <p>it means that even if GFR↑ still it maintains constant fractional reabsorption (two-thirds, or 67%) of the filtered Na⁺ and H₂O</p>	<p>in Thick ascending limb of the loop of Henle 25% of the filtered Na⁺ is reabsorbed</p> <ul style="list-style-type: none"> Contains a Na⁺-K⁺-2Cl⁻ cotransporter in the luminal membrane <p>Thick ascending limb</p> <ul style="list-style-type: none"> Impermeable to water so called diluting segment 	<p>Together reabsorb 8% of the filtered Na⁺.</p> <p>Early DT:</p> <ul style="list-style-type: none"> By Na⁺ - Cl cotransporter impermeable to water so called cortical diluting segment. <p>Late DT and collecting duct.</p> <p>Principal cells reabsorb Na⁺ and H₂O and secrete K⁺.</p> <ul style="list-style-type: none"> alpha Intercalated cells secrete H⁺, or reabsorbs K⁺ by H⁺, K⁺-ATPase 	<p>Carbonic anhydrase inhibitors (e.g., acetazolamide) act on the early PCT to ↓HCO₃ reabsorption</p> <p>Loop Diuretics (furosemide), acts on Thick ascending limb of the loop of Henle inhibit the Na⁺-K⁺-2Cl⁻ cotransporter.</p> <p>Thiazide Diuretics → early DT→ Inhibition of Na⁺-Cl⁻ cotransport</p> <p>Principal Cells→ ADH and aldosterone</p> <p>a-Intercalated cells→ aldosterone</p>
K⁺	Reabsorbs 67% of the filtered K ⁺ along with Na ⁺ and H ₂ O.	Reabsorbs 20% of the filtered K ⁺ . by the Na ⁺ -K ⁺ -2Cl ⁻ cotransporter	<p>Depends on dietary K⁺ intake.</p> <p>low-K⁺ diet (K⁺ depletion) →K⁺ is reabsorbed by an H⁺, K⁺-ATPase in alpha Intercalated cells</p> <ul style="list-style-type: none"> if high K⁺, it secretes K⁺ by principal cells 	<p>Causes of Distal K⁺ Secretion:</p> <ul style="list-style-type: none"> High-K⁺ diet Hyperaldosteronism Alkalosis Thiazide diuretics Loop diuretic
Urea	50% reabsorbed	Secreted here	Impermeable to urea	
Phosphate	85% reabsorbed	No absorption	No absorption	PTH↓ reabsorption
Ca²⁺, Mg²⁺	<ul style="list-style-type: none"> Proximal tubule and thick ascending limb reabsorb more than 90% of the filtered Ca²⁺ by passive processes that are coupled to Na⁺ reabsorption. Mg²⁺ and Ca²⁺ compete for reabsorption So ↑ Ca²⁺ → ↓Mg²⁺ and vice versa 			<p>↑ Ca²⁺ reabsorption</p> <ul style="list-style-type: none"> PTH Thiazide diuretics <p>↓Ca²⁺ reabsorption</p> <ul style="list-style-type: none"> Loop diuretics



Potassium Shifts

Shifts K ⁺ into Cell (Hypokalemia)	Shifts K ⁺ Out Of Cell (Hyperkalemia)
	Digitalis (blocks Na ⁺ /K ⁺ ATPase)
Hypo-osmolarity	Hyperosmolarity
Alkalosis	Lysis of cells (e.g., crush injury, tumor lysis syndrome)
B- agonist	Acidosis
Insulin (Insulin shifts K ⁺ Into cells)	B- blocker
	High blood sugar (insulin deficiency)
	Succinylcholine (↑ risk in burns /muscle trauma)

Hormones acting on Kidneys

Hormone	Action on the Kidneys
PTH	<ul style="list-style-type: none"> ❖ ↓ Phosphate reabsorption (proximal tubule) ❖ ↑ Ca²⁺ reabsorption (distal tubule) ❖ Stimulates 1α-hydroxylase (proximal tubule)
ADH	<ul style="list-style-type: none"> ❖ ↑ H₂O permeability (late distal tubule and collecting duct principal cells)
Aldosterone	<ul style="list-style-type: none"> ❖ ↑ Na⁺ reabsorption (distal tubule principal cells) ❖ ↑ K⁺ secretion (distal tubule principal cells) ❖ ↑ H⁺ secretion (distal tubule α-intercalated cells)
ANP	<ul style="list-style-type: none"> ❖ ↑ GFR ❖ ↓ Na⁺ reabsorption
Angiotensin II	<ul style="list-style-type: none"> ❖ ↑ Na⁺-H⁺ exchange and HCO₃⁻ reabsorption (proximal tubule)

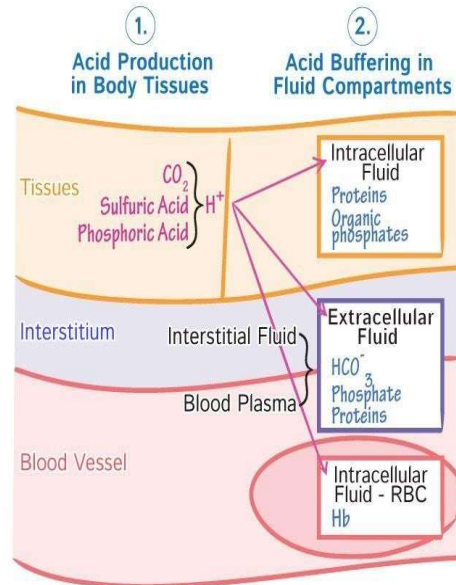
BUFFERS

- Major extracellular (or plasma/interstitial fluid) buffer is bicarbonate (HCO_3^-)
- Minor extracellular buffer is Phosphate (most important urinary buffer)
- Major intracellular buffer is protein (hemoglobin \rightarrow deoxyhemoglobin oxyhemoglobin)
- Other intracellular buffer are Organic phosphates (AMP, ADP, ATP, 2,3-diphosphoglycerate [DPG])
- Exclusive urinary buffer is ammonium.

ACID-BASE REGULATION

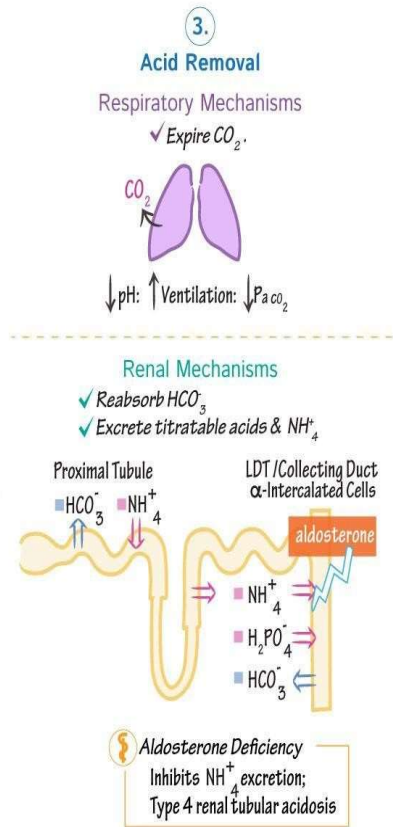
+ Acid Production

- ✓ **Volatile Acid** —
 - ✓ Product of aerobic cellular respiration
 - ✓ CO_2 is expired from the lungs.
- ✓ **Non-volatile Acids** —
 - ✓ Product of protein and phospholipid catabolism.
 - ✓ Examples: sulfuric acid & phosphoric acid
 - ✓ Excreted in urine as titratable acid.
- ✓ **Regulating systems** —
 - ✓ Chemical mixtures (buffers) minimize pH changes.
 - ✓ Respiratory system expires CO_2 .
 - ✓ Urinary system excretes non-volatile acids.
- ✓ Arterial blood plasma pH ≈ 7.4



Acid-Base Imbalance

- ✓ **Alkalosis** — Excessive removal of H^+ ; Blood is more alkaline.
- ✓ **Acidosis** — Excessive addition of H^+ ; Blood is more acidic.



Kidney Endocrine Functions

Erythropoietin

- Released by interstitial cells in peritubular capillary bed in response to hypoxia
- Stimulates RBC proliferation in bone marrow.

Calciferol (vitamin D)

- PCT cells convert 25-OH vitamin D3 (inactive) to 1α -hydroxylase 1.25-(OH) to vitamin D3 (calcitriol active form)

Prostaglandins

- Paracrine secretion vasodilates the afferent arterioles to \uparrow RBF.
- Mnemonic (PDA--Prostaglandins Dilates Afferent arterioles)

Urine Formation

Production of Concentrated Urine	Production of Dilute Urine
<ul style="list-style-type: none"> ❖ Is also called hyperosmotic urine, in which urine osmolarity > blood osmolarity. ❖ Is produced when circulating ADH levels are high (e.g., water deprivation, volume depletion, SIADH). ❖ Mechanism <ul style="list-style-type: none"> ○ Water deprivation → Increases plasma osmolarity Stimulates osmoreceptors in anterior hypothalamus → Increases secretion of ADH from posterior pituitary → Increases water permeability of late distal tubule and collecting duct → Increases water reabsorption → Increases urine osmolarity and decreases urine volume → Decreases plasma osmolarity toward normal 	<ul style="list-style-type: none"> ❖ Is called hypoosmotic urine, in which urine osmolarity < blood osmolarity. ❖ Is produced when circulating levels of ADH are low (e.g., water intake, central DI) or when ADH is ineffective (nephrogenic DI). ❖ Mechanism <ul style="list-style-type: none"> ○ Water intake Decreases plasma osmolarity → Inhibits osmoreceptors in anterior hypothalamus → Decreases secretion of ADH from posterior pituitary → Decreases water permeability of late distal tubule and collecting duct → Decreases water reabsorption → Decreases urine osmolarity and increases urine volume → Increases plasma osmolarity toward normal

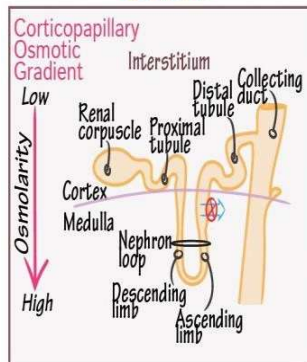
Corticocapillary osmotic gradient **created by** medullary counter current multiplication and **maintained by** Vasa recta & counter current exchange

CORTICOPAPILLARY OSMOTIC GRADIENT

Key Principles

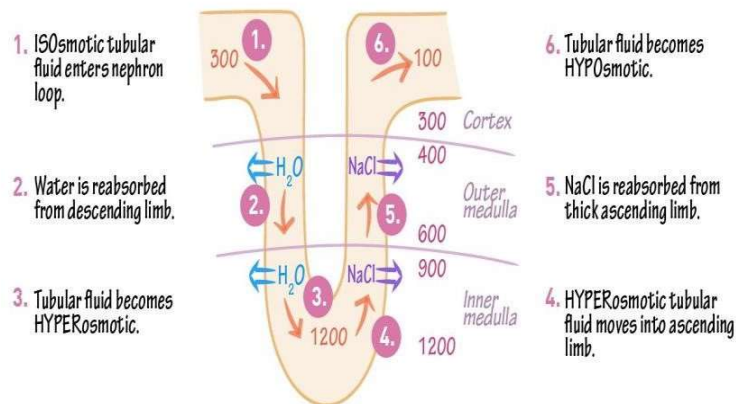
- ✓ Corticopapillary osmotic gradient
- ✓ Osmotic gradient of renal interstitium.
 - Allows nephrons to adjust osmolarity of tubular fluid.
 - Cortex = 300 mOsm/L
 - Medulla = up to 1200 mOsm/L
- ✓ Created by:
 - Medullary countercurrent multiplication
 - Urea recycling
- ✓ Maintained by:
 - Vasa recta and countercurrent exchange.

Overview



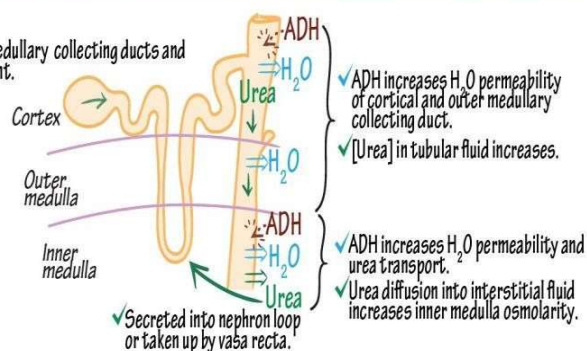
Medullary Countercurrent Multiplication

✓ Thick ascending limb actively pumps NaCl into the medullary interstitium to create osmotic gradient.



Urea Recycling

✓ Urea is reabsorbed from the medullary collecting ducts and contributes to osmotic gradient.
✓ Relies on presence of ADH.



Disorders of ABGs (Acidosis and Alkalosis)

Normal values

pH	7.35-7.45 (below 7.35 is acidic and above 7.45 is alkalosis)
CO ₂	35-45 (less than 35 alkalosis, and above 45 acidosis)
HCO ₃	22-26 below 22 acidosis and above 26 alkalosis)

(5 steps)

Step-1	❖ Is the pH normal? ❖ Look for pH value first and compare whether it is acidic or alkalotic
Step-2	❖ Is the CO ₂ , normal? ❖ Look for CO ₂ , value first and compare whether it is acidic or alkalotic
Step-3	❖ Is the HCO ₃ normal? ❖ Look for HCO ₃ , value first and compare whether it is acidic or alkalotic
Step-4	❖ Match the CO ₂ , or the HCO ₃ , with the pH? ❖ Look for the value which is making the pH acidic or basic. ❖ suppose if pH is acidic and respiratory value is also acidic then the cause is respiratory acidosis and vice versa
Step-5	❖ Does the CO ₂ or the HCO ₃ go the opposite direction of the pH? Next steps look for the value which goes in opposite direction, suppose if pH is acidic, CO ₂ is acidic, and you have made the diagnosis of respiratory acidosis. HCO ₃ is basic, this means compensation has been done and diagnosis will be, respiratory acidosis with metabolic alkalosis.

Example:pH: 7.27 acidotic, CO₂: 53 acidotic, HCO₃: 24 normal

The full diagnosis for this blood gas is: "Uncompensated respiratory acidosis".

Example:pH: 7.60 alkalotic, CO₂: 37 normal, HCO₃: 35 alkalotic

The full diagnosis for this blood gas is "Uncompensated metabolic alkalosis".

Disorder		pH	Primary defect	Compensatory response	Magnitude of compensation
Metabolic acidosis		↓	↓	↓	The pCO ₂ will ↓ by 1 mmHg for every 1 mmol/l for ↓ in HCO ₃
Metabolic alkalosis		↑	↑	↑	The pCO ₂ will ↑ by 1 mmHg for every 1 mmol/l for ↑ in HCO ₃
Respiratory Acidosis	Acute	↓	↑	↑	The HCO ₃ will ↑ by 1 mmol/l for every 10 mmHg ↑ in pCO ₂ above 40 mmHg
	Chronic	↓	↑	↑	The HCO ₃ will ↑ by 4 mmol/l for every 10 mmHg ↑ in pCO ₂ above 40mmHg.
Respiratory alkalosis	Acute	↑	↓	↓	The HCO ₃ will ↓ by 2 mmol/l for every 10 mmHg ↓ in pCO ₂ below 40 mmHg
	Chronic	↑	↓	↓	The HCO ₃ will ↓ by 5 mmol/l for every 10 mmHg ↓ in pCO ₂ below 40 mmHg

Metabolic Acidosis

- ❖ The Anion Gap is used for the evaluation of metabolic acidosis to determine the presence of unmeasured anions.
- ❖ The anion gap is the difference between primary measured Cations (Na⁺) and the primary measured anions (Chloride Cl⁻ and bicarbonate HCO₃⁻) in serum.
 - Anion gap = Na - (Cl + HCO₃)

↑ Anion gap > 12 mEq/L	Normal anion gap 8-12 mEq/L
MUDPILES: <ul style="list-style-type: none"> ❖ Methanol (formic acid) ❖ Uraemia ❖ Diabetic ketoacidosis ❖ Renal ❖ Propylene glycol ❖ Iron tablets or INH ❖ Lactic acidosis ❖ Ethylene glycol ❖ Salicylates (late) 	HARDASS: <ul style="list-style-type: none"> ❖ Hyperalimentation ❖ Addison disease ❖ Renal tubular acidosis ❖ Diarrhea ❖ Acetazolamide ❖ Spironolactone ❖ Saline infusion

Metabolic Alkalosis

Seen with Loop diuretics, Vomiting, Antacid use and Hyperaldosteronism.

Respiratory Acidosis

Airway obstruction, Acute lung disease, Chronic lung disease
Opioids. Sedatives. Weakening of respiratory muscles

Respiratory Alkalosis

- ❖ Hysteria
- ❖ Hypoxemia (e.g., high altitude)
- ❖ Salicylates (early)
- ❖ Tumor
- ❖ Pulmonary embolism

RENAL DISORDERS

NEPHROTIC SYNDROME

Includes a group of conditions characterized by increased basement membrane permeability.

Characteristic features:

- Massive proteinuria (daily loss of > 3.5 grams of protein per day).
- Hypoalbuminemia (serum albumin less than 3 g/100 mL)
- Generalized edema
- Hyperlipidemia and hypercholesterolemia are caused by increased hepatic lipoprotein synthesis.

Causes:

- Primary glomerular disease: Minimal change disease, Membranous GN, Focal segmental glomerulosclerosis.
- Systemic diseases: SLE, Amyloidosis, Diabetic nephropathy

Minimal change disease (Lipoid Nephrosis)	<ul style="list-style-type: none">❖ Most common cause of Nephrotic syndrome in children❖ Light microscopy: normal-appearing glomeruli.❖ Electron microscopy → effacement or fusing of podocytes foot processes.❖ Excellent response to corticosteroids❖ Albumin is lost mostly, while, sparing the other proteins❖ Associations: Hodgkin's lymphoma, vaccination, EBV, NSAIDs								
Membranous nephropathy (membranous glomerulonephritis)	<ul style="list-style-type: none">❖ Most common cause of Nephrotic syndrome in adults❖ Light microscopy: diffuse capillary and GBM thickening❖ Electron microscopy→ "spike and dome" appearance with Subepithelial deposits. Poor response to corticosteroids❖ Associations:<ul style="list-style-type: none">○ SLE (10%), hepatitis B, syphilis, malaria infection: drugs (gold salts or Penicillamine); or malignancy.○ The disorder sometimes causes renal vein thrombosis, because of loss of antithrombin III, protein C and S & ↑ fibrinogen								
Focal segmental glomerulosclerosis	<ul style="list-style-type: none">❖ It is more common in African Americans and is associated with HIV, obesity, heroin abuse.❖ It is characterized by sclerosis of some glomeruli, in these affected glomeruli only a portion of capillary tuft is involved.❖ Massive proteinuria occurs❖ Light Microscopy → segmental sclerosis❖ Electron Microscopy→ effacement of foot process/Podocyte effusion (same as Minimal change disease, but minimal change > focal segmental sclerosis)								
Diabetic nephropathy	<ul style="list-style-type: none">❖ ↑in mesangial matrix → two patterns:<ul style="list-style-type: none">○ Diffuse glomerulosclerosis → diffusely increase in mesangial matrix.○ Nodular glomerulosclerosis→ nodular accumulations of mesangial matrix material (Kimmelstiel-Wilson nodules).❖ Electron microscopy: ↑in thickness of the glomerular basement membrane								
Renal Amyloidosis	<ul style="list-style-type: none">❖ Amyloidosis refers to accumulation of insoluble fibrillary proteins that form β-pleated sheaths, two types.❖ Light Microscopy---Congo red stain shows apple-green birefringence.								
	<table><tr><th>Primary (AL) amyloidosis</th><th>Secondary (AA) amyloidosis</th></tr><tr><td>Most common in developed world.</td><td>Less common in developed countries</td></tr><tr><td>Due to deposition of proteins from la Light chains</td><td>Occurs in patients with long-standing neoplasia or inflammation and is associated with serum amyloid protein called AA protein</td></tr><tr><td>Can occur as a plasma cell disorder or associated with multiple myeloma and Waldenström macroglobulinemia</td><td>It is often seen in concert with tuberculosis, leprosy. RA</td></tr></table>	Primary (AL) amyloidosis	Secondary (AA) amyloidosis	Most common in developed world.	Less common in developed countries	Due to deposition of proteins from la Light chains	Occurs in patients with long-standing neoplasia or inflammation and is associated with serum amyloid protein called AA protein	Can occur as a plasma cell disorder or associated with multiple myeloma and Waldenström macroglobulinemia	It is often seen in concert with tuberculosis, leprosy. RA
	Primary (AL) amyloidosis	Secondary (AA) amyloidosis							
	Most common in developed world.	Less common in developed countries							
	Due to deposition of proteins from la Light chains	Occurs in patients with long-standing neoplasia or inflammation and is associated with serum amyloid protein called AA protein							
Can occur as a plasma cell disorder or associated with multiple myeloma and Waldenström macroglobulinemia	It is often seen in concert with tuberculosis, leprosy. RA								

NEPHRITIC SYNDROME

(Nephritic) Inflammatory rupture of the glomerular capillaries, with resultant bleeding

Characterized features: (A HOPE)

- Azotemia, Hematuria, Hypertension, Oliguria, Proteinuria (less than 3g/day), Edema

Acute post streptococcal glomerulonephritis	<ul style="list-style-type: none"> ❖ Most common type of post-infectious glomerulonephritis in children's ❖ Occurs 1-4 weeks after a sore throat caused by group A B-hemolytic streptococci i.e., streptococcus pyogenes. Type II hypersensitivity. ❖ Clinical features: <ul style="list-style-type: none"> ○ Sudden onset of fever, oliguria, hematuria (cocoa-colored urine) ❖ Findings: <ul style="list-style-type: none"> ○ Serum C3 decreased. ASO titres elevated. ○ Light microscopy: glomeruli enlarged + hypercellular. ○ Electron microscopy → Subepithelial humps ○ Immunofluorescence → lumpy bumpy appearance
Rapidly progressive (crescentic) glomerulonephritis	<p>Nephritic syndrome that progresses rapidly to renal failure within weeks or months. Light microscopy & Immunofluorescence → Crescent shape glomerulonephritis. Disease processes that may result in this pattern are.</p> <div> <p>Good pasture syndrome</p> <ul style="list-style-type: none"> ○ Type II hypersensitivity reaction caused by antibodies against GBM and alveolar basement membrane. ○ IgG deposits on renal biopsy ○ Involves lung and renal vessels ○ Hemorrhagic pneumonitis (pneumonia plus hemoptysis) ○ Nephritic syndrome </div>
IgA Nephropathy (Berger disease)	<ul style="list-style-type: none"> ❖ Most common type of nephritic syndrome overall and is due to deposition of IgA in the mesangium. ❖ It presents with recurrent episodes of hematuria following upper RTI, GI infections, occurs 1-2 days after infection. ❖ Associations: coeliac disease/dermatitis herpetiformis. Henoch-Scholein purpura ❖ Light microscopy → mesangial expansion ❖ Immunofluorescence → granular mesangial IgA and lambda light chain deposition ❖ Not to be confused with Buerger disease (Thromboangiitis obliterans).
Alport syndrome	<ul style="list-style-type: none"> ❖ Most commonly X-linked dominant. ❖ Defective glomerular basement membrane synthesis due to abnormal collagen type IV ❖ Clinical features: Mnemonic: "can't see, can't pee, and can't hear a bee." <ul style="list-style-type: none"> ○ Eye problems (e.g., retinopathy, lens dislocation) ○ Glomerulonephritis ○ Sensorineural deafness ❖ Electron microscopy → "Basket-weave" appearance.

Nephritic-Nephrotic syndrome

- ❖ Severe nephritic syndrome with profound GBM damage that damages the glomerular filtration charge barrier → nephrotic-range proteinuria (>3.5g/day) and concomitant features of nephrotic syndrome. Can occur with any form of nephritic syndrome, but is most seen with:
 - Membranoproliferative glomerulonephritis (MPGN) (also known as mesangiocapillary glomerulonephritis).
 - MPGN is a nephritic syndrome that often co-presents with nephrotic syndrome.

	Type I MPGN "Subendothelial Immune Complex"	Type II MPGN "Dense Deposit Disease"
Cause	❖ Immune complex nephritis	❖ Also known as dense deposit disease, associated with C3 nephritic factor
Mechanism	❖ It results from activation of both classic and alternate complement pathway	❖ It results from activation of only alternate complement pathway. ❖ C3 nephritic factor, which is an autoantibody that prevents degradation of C3-convertase causing sustained activation of C3, resulting in very low C3 levels
Causes	❖ May be 2° to hepatitis B or C infection. ❖ Idiopathic ❖ cryoglobulinemia	❖ Partial lipodystrophy ❖ Factor H deficiency
H&E stain	Tram track appearance	Tram track appearance
EM	Subendothelial deposits	Intramembranous deposits

Key Facts

- ❖ IgA nephropathy- Mesangial deposits in glomerular basement membrane
- ❖ IgM and C3 deposits in= FSGS (focal segmental glomerulosclerosis) associated with HIV
- ❖ Linear deposits= Goodpasture syndrome
- ❖ Subepithelial deposits/humps= post streptococcal GN
- ❖ Subendothelial deposits = SLE and Membranoproliferative glomerulonephritis (MPGN) type-1
- ❖ Spike and Dome are seen in = Membranous glomerulonephritis - (associated with SLE. Hep B)
- ❖ Selective proteinuria= Minimal change disease
- ❖ Alport syndrome = "Basket-weave" appearance.
- ❖ Post-streptococcal glomerulonephritis occurs 1-2 weeks following infection (URTI). C3 is low
- ❖ IgA nephropathy occurs 1-2 days after infection (URTI)

SLE Renal Complications

- ❖ WHO classification
 - Class 1: normal kidney
 - Class II: mesangial glomerulonephritis
 - Class III: focal (and segmental) proliferative glomerulonephritis
 - Class IV: **diffuse proliferative glomerulonephritis--- most common and severe form.**
 - Class V: diffuse membranous glomerulonephritis
 - Class VI: sclerosing glomerulonephritis

KIDNEY STONES

- ❖ Features → flank pain (which is colicky, radiating to groin), hematuria.
- ❖ Complications → pyelonephritis, hydronephrosis
- ❖ Types

Calcium stones	Ammonium magnesium phosphate (struvite)	Uric acid	Cysteine
<ul style="list-style-type: none"> ❖ Most common (80%) ❖ Calcium oxalate more common than calcium phosphate stones. 	2 nd common (15%) of stones.	About 5% of all stones.	Less common
<ul style="list-style-type: none"> ❖ Caused by: <ul style="list-style-type: none"> ▪ Ethylene glycol (antifreeze) ingestion ▪ Vitamin C abuse ▪ Hypercalcemia which may be caused by hyperparathyroidism malignancy, sarcoidosis, vitamin D intoxication, and the milk-alkali syndrome. 	<ul style="list-style-type: none"> ❖ Caused by <ul style="list-style-type: none"> ▪ Urease bugs (e.g., Proteus Staphylococcus Saprophyticus, Klebsiella) that hydrolyse urea to ammonia → urine alkalization. ❖ Commonly form staghorn calculi 	<ul style="list-style-type: none"> Caused by: <ul style="list-style-type: none"> ▪ Strong association with Hyperuricemia (e.g., gout) ❖ Often seen in leukemia. 	<ul style="list-style-type: none"> Caused by Cystine-reabsorbing PCT transporter loses function, causing cystinuria. Results in poor reabsorption of Ornithine, Lysine, Arginine (COLA). Can form staghorn calculi.
Envelop shaped	Coffin lid shaped	Rhomboid or rosettes	Hexagonal shape
Radiopaque	Radiopaque	Radiolucent	Radiolucent
Treatment: Low-sodium diet Thiazides Citrate	<ul style="list-style-type: none"> ❖ Treatment: <ul style="list-style-type: none"> ▪ Eradication of underlying infection ▪ Surgical removal of stone 	<ul style="list-style-type: none"> ❖ Treatment: <ul style="list-style-type: none"> ▪ Alkalinization of urine ▪ Allopurinol. 	<ul style="list-style-type: none"> ❖ Treatment: <ul style="list-style-type: none"> ▪ Alkalinization of urine ▪ Low sodium diet ▪ Chelating agents if refractory.

RENAL CYST DISORDERS

Autosomal dominant polycystic kidney disease (ADPKD)

- ❖ Numerous cysts in cortex and medulla causing bilateral enlarged kidneys-ultimately destroy kidney parenchyma.
- ❖ Autosomal dominant, in which renal parenchyma is replaced by cyst
- ❖ Manifests between 15 and 30 years of age, even though the genetic defect is present at birth. The disease occurs bilaterally, the kidneys are greatly enlarged.
- ❖ Clinical features:
 - Presents with flank pain, hematuria, hypertension, urinary infection, progressive renal failure (50% of individuals).
- ❖ Types:

ADPKD Type 1	ADPKD Type 2
85% of cases	15% of cases
Mutation in PKD1 (which code for polycystin-1)	Mutation in PKD2 (which code for polycystin-2)
Chromosome 16	Chromosome 4

- ❖ Ultrasound diagnostic criteria (in patients with positive family history)
 - Two cysts, unilateral or bilateral, if aged < 30 years
 - Two cysts in both kidneys if aged 30-59 years
 - Four cysts in both kidneys if aged > 60 years
- ❖ Features: Hypertension, recurrent UTIs, abdominal pain, renal stones, CKD
- ❖ Extra-renal manifestations
 - Liver cysts (70%), Berry aneurysms of the circle of Willis (8%)
 - Cardiovascular system: MVP. aortic dilation and dissection
- ❖ Treatment: ACE inhibitors or ARBS.

Autosomal Recessive Polycystic Kidney Disease	<ul style="list-style-type: none"> ❖ Cystic dilation of collecting ducts. ❖ Often presents in infancy. ❖ Associated with <ul style="list-style-type: none"> ○ Congenital hepatic fibrosis. ○ Significant oliguric renal failure in utero can lead to Potter sequence. ❖ Death from this recessive disorder results shortly after birth. 	
Medullary Cystic Disease	<ul style="list-style-type: none"> ❖ Inherited disease causing tubulointerstitial fibrosis and progressive renal insufficiency with inability to concentrate urine. ❖ Medullary cysts usually not visualized, shrunken kidneys on ultrasound. ❖ Poor prognosis 	
Simple Vs Complex Renal Cysts	Simple Renal Cysts	Complex Renal Cysts
	❖ Filled with ultrafiltrate	Solid components on imaging
	❖ Very common	Less common comparatively
	❖ Found incidentally and typically asymptomatic	Require follow-up or removal due to risk of renal cell carcinoma

URINARY TRACT INFECTIONS (UTIS)

Cystitis

Definition	Inflammation of urinary bladder. usually defined as more than 10 ⁵ organisms Per milliliter of mid-urine sample
Clinical features	Presents as suprapubic pain, dysuria, urinary frequency, urgency, Pyuria (neutrophils)
Risk factors	Female gender (short urethra), sexual intercourse ("honeymoon cystitis"), indwelling catheter, diabetes mellitus, impaired bladder emptying
Causes	<ul style="list-style-type: none"> ❖ E coli (most common). ❖ Staphylococcus Saprophyticus seen in sexually active young women (E coli is still the most common in this group). ❖ Klebsiella. ❖ Proteus mirabilis- urine has ammonia scent.

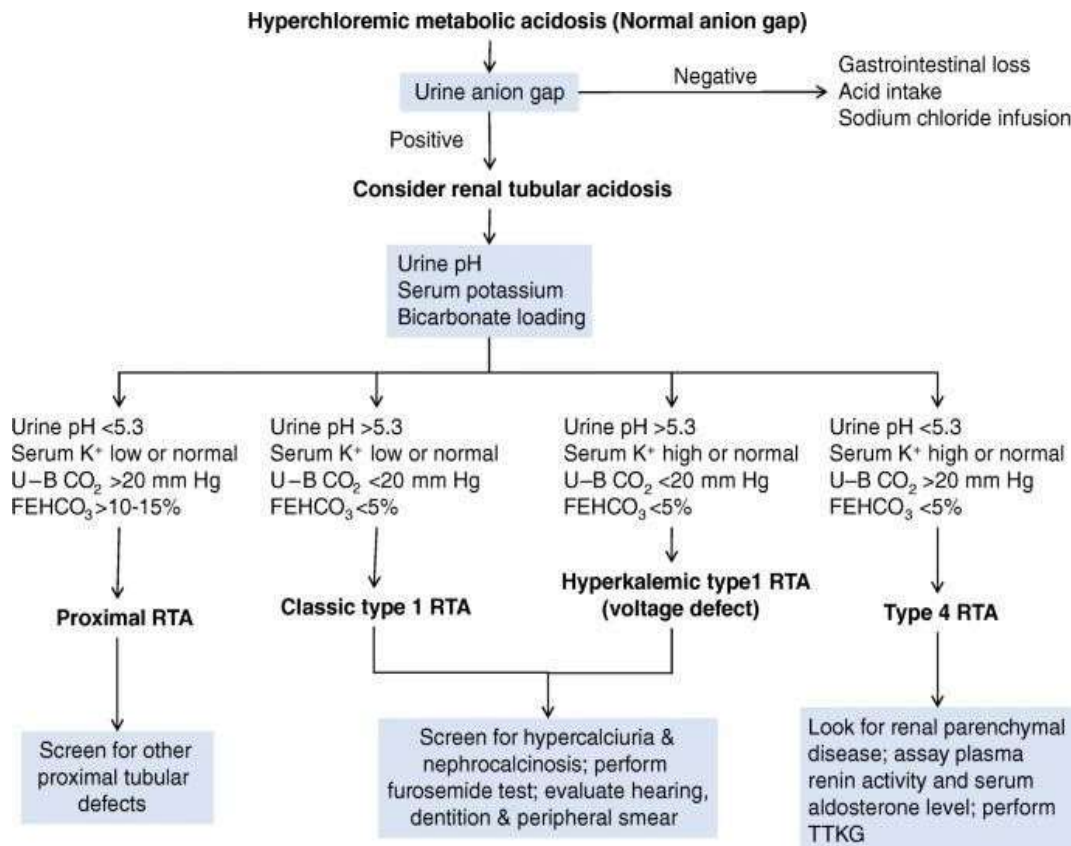
Pyelonephritis

Acute Pyelonephritis	<ul style="list-style-type: none"> ❖ Neutrophils infiltrate renal interstitium. Affects cortex with relative sparing of glomeruli/vessels. ❖ Clinical features: <ul style="list-style-type: none"> ○ Fever, flank pain, nausea/vomiting, chills. ❖ Causes includes. <ul style="list-style-type: none"> ○ Ascending UTI (E. coli is most common) ❖ Risk factors: Diabetes mellitus, pregnancy, indwelling urinary catheter, urinary tract obstruction. ❖ Complications: Chronic pyelonephritis, renal papillary necrosis, perinephric abscess, urosepsis. ❖ Treatment: IV Antibiotics followed by oral.
Chronic Pyelonephritis	<ul style="list-style-type: none"> ❖ Coarse, asymmetric corticomedullary scarring, blunted calyx. ❖ Atrophic tubules can contain eosinophilic casts resembling thyroid tissue (thyroidization of kidney) ❖ <u>Causes</u>: Chronic urinary tract obstruction and repeated bouts of acute inflammation ❖ <u>Complications</u>: Renal hypertension and end-stage renal disease. ❖ <u>Xanthogranulomatous pyelonephritis</u> <ul style="list-style-type: none"> ○ Rare, Grossly orange nodules that can mimic tumor nodules. ○ Characterized by widespread kidney damage due to granulomatous tissue containing foamy macrophages.

RENAL TUBULAR ACIDOSIS

A disorder of the renal tubules that leads to normal anion gap (hyperchloremic) metabolic acidosis.

	Distal renal tubular acidosis (type 1)	Proximal renal tubular acidosis (type 2)	Hyperkalemia renal tubular acidosis (type 4)
Defect	Defect in ability of alpha intercalated cells to secrete H^+ no new HCO_3^-	Defect in PCT HCO_3^- reabsorption	\downarrow aldosterone production causes hyperkalemia $\rightarrow \downarrow$ NH_3 synthesis in PCT leads to \downarrow NH_4^+ excretion
Urine pH	> 5.5	< 5.5	< 5.5
Serum K^+	Hypokalemia	Hypokalemia	Hyperkalemia
Causes	Amphotericin B toxicity congenital obstruction of urinary tract	Fanconi syndrome and carbonic anhydrase Inhibitors	Diabetes, ACE inhibitors, ARBS, NSAIDS



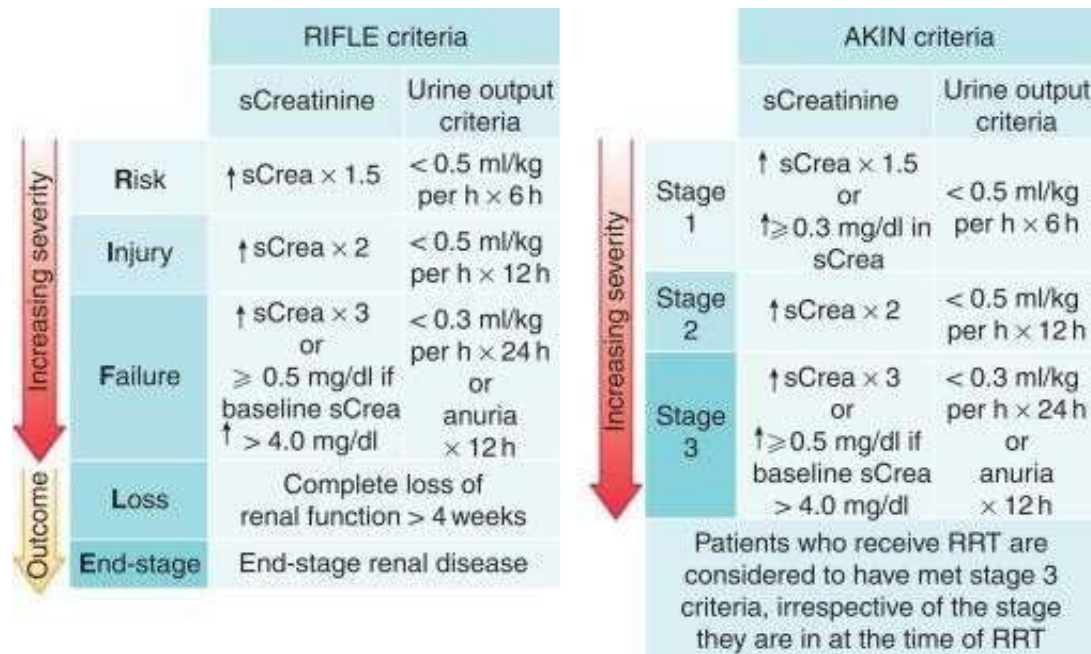
ACUTE KIDNEY INJURY (ACUTE RENAL FAILURE)

Acute and reversible deterioration of renal function which develops over periods of days to weeks and measure by \uparrow creatinine and \uparrow BUN or by oliguria/anuria.

Pre-renal causes	<ul style="list-style-type: none"> ❖ Heart failure, Blood loss, Fluid loss ❖ Renal artery stenosis or occlusion
Intrinsic renal causes	<ul style="list-style-type: none"> ❖ Acute tubular necrosis, Interstitial disease ❖ Characterized by antibodies and eosinophils attacking cells lining the tubules. ❖ Primary and secondary glomerulonephritis
Post-renal causes	<ul style="list-style-type: none"> ❖ Obstruction because of Stones, Tumors, Inflammation, Prostate enlargement

In Prerenal causes- kidneys hold on to sodium to preserve volume.

	Pre-Renal	Intrinsic	Post-Renal
Urine osmolality (mOsm/kg)	>500	<350	<350
Urine Na ⁺ (mEq/L)	<20	>40	>40
FE _{Na}	<1%	>2%	<1%(mild) >2%(severe)
Serum BUN/Cr	>20	<15	Varies



Consequences of Renal Failure

Inability to make urine and excrete nitrogenous wastes.

- Metabolic Acidosis
- Dyslipidemia (especially ↑ triglycerides)
- Hyperkalemia, Hypocalcemia (↓ active form of vitamin D)
- Uremia--clinical syndrome marked by ↑ BUN (Nausea, anorexia, encephalopathy)
- Na⁺/H₂O retention (HF, pulmonary edema, hypertension)
- Growth retardation and developmental delay
- Erythropoietin failure (anemia) – give subcutaneous erythropoietin
- Renal osteodystrophy

TUBULO- INTERSTITIAL DISORDERS OF THE KIDNEY

Acute Interstitial nephritis (Tubulointerstitial nephritis)

- ❖ Acute interstitial renal inflammation
- ❖ Pyuria (classically eosinophils) and azotemia occurring after administration of drugs.
- ❖ Causes (Mnemonic Remember these P's)
 - Pee (diuretics)
 - Pain-free (NSAIDs)
 - Penicillin's and cephalosporins
 - Proton pump inhibitors
 - Rifampin
 - Other Processes such as autoimmune diseases (eg, Sjögren syndrome SLE, sarcoidosis)
- ❖ The nephritis resolves on cessation of exposure to the inciting drug

Renal papillary necrosis (necrotizing papillitis)	<ul style="list-style-type: none"> ❖ Ischemic necrosis of the tips of the renal papillae → gross hematuria and proteinuria. ❖ May be triggered by recent infection or immune stimulus. ❖ Associated with: (Mnemonic: SAAD papa with papillary necrosis) <ul style="list-style-type: none"> ○ Sickle cell disease or trait ○ Acute pyelonephritis ○ Analgesics (NSAIDs) ○ Diabetes mellitus 								
Acute tubular necrosis (ATN)	<ul style="list-style-type: none"> ❖ Is the most common cause of acute renal failure and most common cause of acute kidney injury in hospitalized patients. ❖ This condition is reversible but if left untreated can be fatal, especially during initial oliguric phase. ❖ Key finding: granular ("muddy brown") casts ❖ Can be caused by ischemic or nephrotoxic injury. <table border="1"> <thead> <tr> <th>Ischemic Injury</th><th>Nephrotoxic Injury</th></tr> </thead> <tbody> <tr> <td>Secondary to renal blood flow</td><td>Secondary to injury resulting from toxic substances.</td></tr> <tr> <td>Examples: <ul style="list-style-type: none"> ○ Hypotension, shock, sepsis, hemorrhage, HF </td><td>Examples: <ul style="list-style-type: none"> ○ Aminoglycosides, radiocontrast agents, lead, cisplatin, crush injury (myoglobinuria), ethylene glycol, hemoglobinuria </td></tr> <tr> <td>PCT and thick ascending limb are highly susceptible to injury</td><td>PCT is particularly susceptible to injury.</td></tr> </tbody> </table>	Ischemic Injury	Nephrotoxic Injury	Secondary to renal blood flow	Secondary to injury resulting from toxic substances.	Examples: <ul style="list-style-type: none"> ○ Hypotension, shock, sepsis, hemorrhage, HF 	Examples: <ul style="list-style-type: none"> ○ Aminoglycosides, radiocontrast agents, lead, cisplatin, crush injury (myoglobinuria), ethylene glycol, hemoglobinuria 	PCT and thick ascending limb are highly susceptible to injury	PCT is particularly susceptible to injury.
Ischemic Injury	Nephrotoxic Injury								
Secondary to renal blood flow	Secondary to injury resulting from toxic substances.								
Examples: <ul style="list-style-type: none"> ○ Hypotension, shock, sepsis, hemorrhage, HF 	Examples: <ul style="list-style-type: none"> ○ Aminoglycosides, radiocontrast agents, lead, cisplatin, crush injury (myoglobinuria), ethylene glycol, hemoglobinuria 								
PCT and thick ascending limb are highly susceptible to injury	PCT is particularly susceptible to injury.								

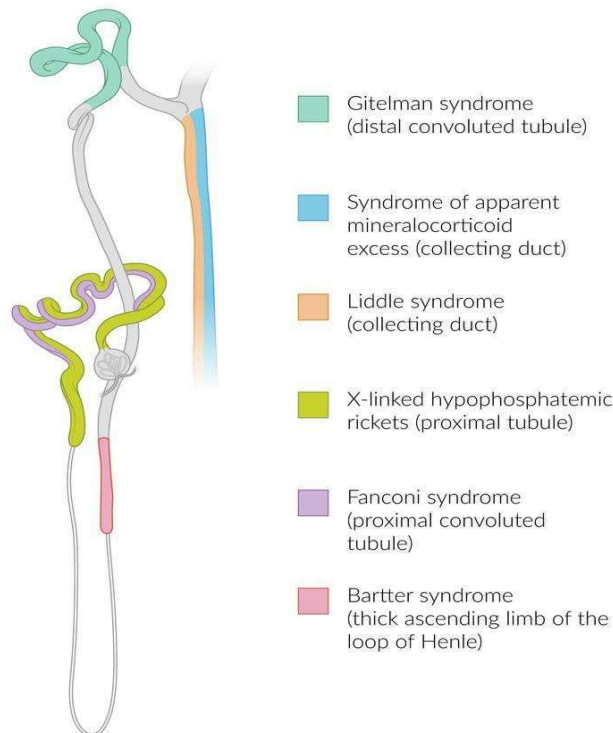
HYDRONEPHROSIS

Definition	❖ Progressive dilation of the renal pelvis and calyces
Causes	<ul style="list-style-type: none"> ❖ Urinary tract obstruction (e.g., renal stones, severe BPH, cervical cancer) ❖ Retroperitoneal fibrosis ❖ Vesicoureteral reflux
Findings	<ul style="list-style-type: none"> ❖ Dilation occurs proximal to site of pathology. ❖ Serum creatinine becomes elevated if obstruction is bilateral or if patient has only one kidney. ❖ Leads to compression and possible atrophy of renal cortex and medulla
Treatment	<ul style="list-style-type: none"> ❖ Hydronephrosis can be physiologic. Treatment should be guided at improving symptoms, treating infections, or improving renal function. ❖ Urgent treatment may require percutaneous nephrostomy tube or ureteral stenting to relieve pressure

DISORDERS OF RENAL TUBULAR FUNCTION

Fanconi syndrome	<ul style="list-style-type: none"> ❖ This manifestation of generalized dysfunction of the proximal renal tubules may be hereditary or acquired. ❖ Impaired reabsorption of glucose (glycosuria), amino acids (aminoaciduria), phosphate (hypophosphatemia), and bicarbonate (systemic acidosis) is characteristic. ❖ Causes: <ul style="list-style-type: none"> ○ Hereditary defects (e.g., Wilson disease, glycogen storage disease). ○ Ischemia ○ Multiple myeloma ○ Nephrotoxins/drugs (e.g., cisplatin, tenofovir), lead poisoning
Hartnup disease	<ul style="list-style-type: none"> ❖ This impaired tubular reabsorption of tryptophan is genetically determined. ❖ This condition leads to pellagra-like manifestations

Congenital Syndromes	Bartter's syndrome	Gitelman's syndrome	Liddle's syndrome
	❖ Autosomal recessive	❖ Autosomal recessive	❖ Autosomal dominant
	❖ It is due to defective chloride absorption at the $\text{Na}^+ \text{K}^+ 2\text{Cl}^-$ cotransporter in the ascending loop of Henle (like furosemide-think of this disease as like taking large doses of furosemide)	❖ Is due to a defect in the thiazide-sensitive $\text{Na}^+ \text{Cl}^-$ transporter in the distal convoluted tubule.	❖ Disordered sodium channels in the distal tubules leading to increased reabsorption of sodium. (like hyperaldosteronism)
	❖ Normotension ❖ severe hypokalemia	❖ Normotension ❖ Hypokalemia+ Hypomagnesaemia	❖ Hypertension Hypokalemia
	❖ Note: It should be noted that it is associated with normotension (unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome which are associated with hypertension).		❖ Treatment: Amiloride or triamterene



CHRONIC KIDNEY DISEASE (CKD)

Definition

- ❖ Impaired renal function for 3 months based on abnormal structure or function.
OR

Causes

- ❖ GFR <60mL/min for 3 months with or without evidence of kidney damage.
- ❖ Inherited causes
 - Adult polycystic kidney disease-most common
 - Alport's syndrome
 - Fabry's disease
- ❖ Acquired causes:
 - DM Type II >> Type I-Most common
 - Hypertension or renovascular disease
 - Pyelonephritis
 - Glomerulonephritis (commonly IgA nephropathy, systemic disorders, eg SLE vasculitis)
 - Unknown: up to 20% in the UK have no obvious cause of CKD

Classification

Stage	GFR (mL/min)	Notes
1	>90	Normal or ↑GFR with other evidence of renal damage
2	60-89	Slight↓ GFR with other evidence of renal damage
3A	45-59	Moderate↓ GFR with or without evidence of other renal damage
3B	30-44	
4	15-29	Severe↓ GFR with or without evidence of renal damage
5	<15	Established renal failure

Labs

- ❖ Hb (normochromic, normocytic anemia), ESR, U&E, glucose (DM),
- ❖ ↓Ca²⁺, ↑PO₄³⁻ ↑ alkaline Phosphatase (renal osteodystrophy).
- ❖ ↑PTH if CKD stage 3 or more

Treatment

- ❖ Limiting progression/complications
 - BP:
 - Target BP is <130/80 (<125/75 if diabetic or ACR >70).
 - Drug of choice-ACE-inhibitors or ARB
 - Renal bone disease (risk of osteodystrophy or adynamic bone disease);
 - Check PTH and treat if raised.
 - PO₄³⁻ rises in CKD, which PTH further.
 - Restrict diet, give binders to gut absorption.
 - Vit D analogues (eg alfacalcidol) and Ca²⁺ supplements bone disease and hyperparathyroidism
 - Cardiovascular:
 - Most common cause of death
 - Give statins & aspirin also (CKD is not a contraindication to the use of low - dose aspirin but beware of risk of bleeding).

Diet:

- Moderate protein diet, K⁺ restriction if hyperkalemic, and avoidance of high phosphate foods (eg milk, cheese, eggs).

❖ Symptom control

Anemia:

- Replace iron/B12/folate if necessary.
- If still anaemic consider recombinant human erythropoietin. There are many formulations.

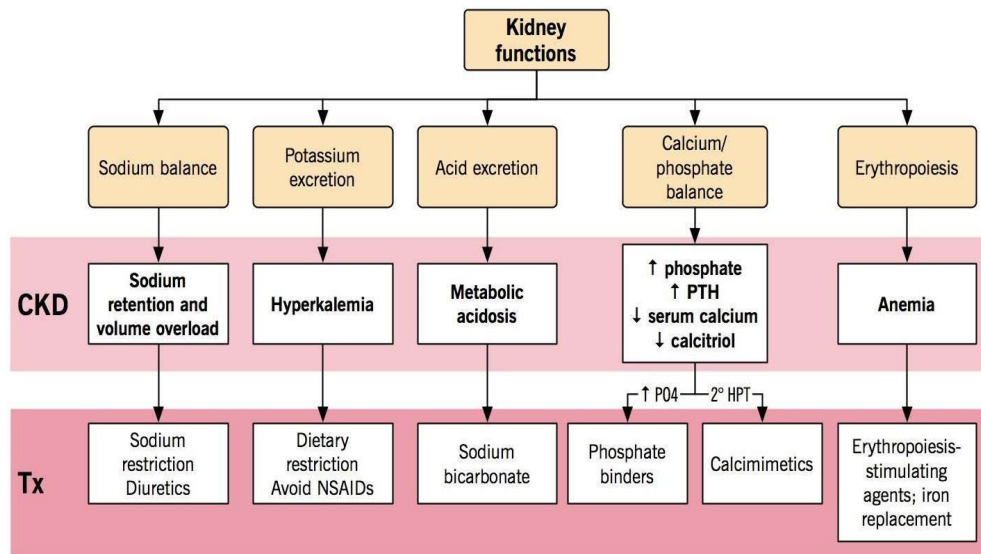
Acidosis:

- Sodium bicarbonate supplements for patients with low serum level

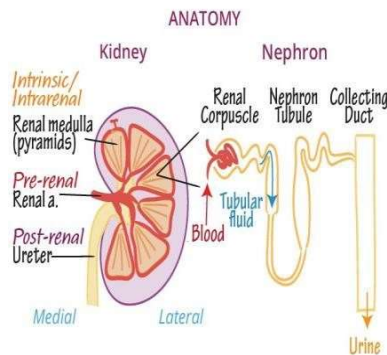
○ Edema:

- High doses of loop diuretics may be needed.
- Restriction on fluid and sodium intake.

Complications of CKD



RENAL PATHOLOGY OVERVIEW



RENAL FAILURE

Excess retention of nitrogenous waste products & electrolyte disturbances

- Metabolic Acidosis
- Dyslipidemia
- Hyperkalemia
- Uremia
- Na⁺/H₂O retention (w/HF, pulm. edema, HTN)
- Growth retardation/dev. delay
- Erythropoietin deficiency (anemia)
- Renal osteodystrophy

ACUTE KIDNEY INJURY: ↑ Creatinine ↓ Urine volume.

Pre-renal (hemodynamics):

- Intravascular volume depletion
- Bilateral renal stenosis
- Heart failure
- ACE inhibitors, ARBs
- Hypotension

Intrinsic/Intrarenal

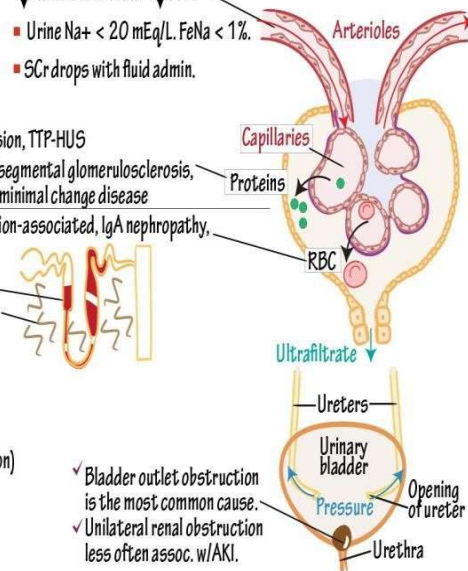
- Vascular: vasculitis, malignant hypertension, TTP-HUS
- Glomerular: Nephrotic syndrome: focal segmental glomerulosclerosis, membranous nephropathy, minimal change disease
- Nephritic syndrome: Infection-associated, IgA nephropathy, Anti GBM, etc.
- Tubular: Acute tubular necrosis
- Interstitial: Acute Interstitial nephritis
- Urine Na⁺ > 40 mEq/L, FeNa > 2%.

Post-renal (obstructive)

- Congenital: renal dysplasia
- Tumors (prostate, etc. cause compression)
- Stones: calcium, ammonium magnesium phosphate, uric acid, cystine.
- Infection

Azotemia = Inc Blood Urea Nitrogen (BUN), creatinine, other waste products in the blood.

- Renal Blood Flow = ↓ GFR.
- Urine Na⁺ < 20 mEq/L, FeNa < 1%.
- SCr drops with fluid admin.



CHRONIC KIDNEY INJURY

- Diabetes
- 1° Glom. nephritis
- Hypertension (2° Glom. nephritis)
- AD polycystic kidney disease

Uremia = Azotemia that leads to cluster of signs/symptoms in various body systems. Usually in CKI, can be AKI

End-Stage Renal Disease = GFR is < 5% normal, terminal stage of uremia.

TUMORS**Renal cell carcinoma (RCC)**

Origin	❖ PCT cells
Incidence	❖ Most common renal malignancy and most common in men 50-70 years
Association	❖ Gene deletion on chromosome 3 (RCC-3 letters Chromosome 3)
Presenting features	❖ Flank pain, palpable mass, and hematuria, fever, Secondary polycythemia ❖ Associated with paraneoplastic syndromes (eg: ectopic EPO, ACTH, PTHrP, renin).
Invades	❖ renal vein (may develop Varicocele if left sided) then IVC and spreads hematogenously
Metastasis	❖ To Lungs and bone

Nephroblastoma (Wilms Tumor)

Origin	❖ From primitive metanephric tissue
Incidence	❖ Most common renal malignancy of early childhood. ❖ Incidence peaks in children 2 to 4 years of age.
Association	❖ Mutations of tumor suppressor genes WT1 or WT2 on chromosome 11.
Features	❖ Presents with large, palpable, unilateral flank mass and/or hematuria
Association with syndromes	<p><u>WAGR complex</u></p> <ul style="list-style-type: none"> ○ Wilms tumor, Aniridia (absence of iris), Genitourinary malformations, mental Retardation/intellectual disability ○ Associated with deletion WT-1 tumor suppressor gene. <p><u>Denys-Drash:</u></p> <ul style="list-style-type: none"> ○ Wilms tumor, early-onset nephrotic syndrome, male pseudohermaphroditism ○ Associated with abnormalities of WT1 gene. <p><u>Beckwith-Wiedemann:</u></p> <ul style="list-style-type: none"> ○ Wilms tumor, macroglossia, organomegaly, hemihyperplasia ○ Associated with mutation of WT2 gene.

Transitional Cell Carcinoma

- ❖ Most common tumor of urinary tract system
- ❖ Can occur in renal calyces, renal pelvis, ureters, and bladder.
- ❖ Can be suggested by painless hematuria (no casts).
- ❖ Associated with problems in your Pee. **SAC:** Phenacetin, Smoking, Aniline dyes, and Cyclophosphamide.

Squamous Cell Carcinoma of the Bladder

- ❖ Chronic Irritation of urinary bladder → squamous metaplasia → dysplasia and squamous cell carcinoma.
- ❖ Risk factors include Schistosoma haematobium (S for Squamous cell carcinoma= S for Schistosoma haematobium) infection, smoking, chronic nephrolithiasis.
- ❖ Presents with painless hematuria.

Causes of Sterile Pyuria

- ❖ Partially treated UTI
- ❖ Urethritis e.g., Chlamydia
- ❖ Renal tuberculosis
- ❖ Renal stones
- ❖ Appendicitis
- ❖ Bladder/renal cell cancer
- ❖ Adult polycystic kidney disease

HIGH YEILD + PAST PAPERS BCQS

1. ECF is measured by = Inulin. Plasma measured by Evans blue, TBW measured by D2O/Antipyrine.
2. Interstitial fluid = 11 Lit. ECF = 28 L. TBW in 70kg man is 42 Liter.
3. Water travels from plasma to interstitium through = filtration. Water enters the cell by = pores
4. Autoregulation of kidney is done by = Tubulo-glomerular feedback system
5. Short action of angiotensin II = Vasoconstriction
6. Which hormone maintains water & electrolytes balance = Aldosterone.
7. ADH regulates plasma volume and urine osmolarity
8. Decrease Lymphatic flow due to: = Increase Plasma oncotic Pressure
9. Nephropathy is diagnosed by: =Microalbuminuria
10. Loss of thirst due to: =Low plasma osmolarity
11. JG nephrons most imp function is = counter current multiplier
12. Estimation of GFR is done via = Creatinine clearance
13. Urine specific gravity indicates: = Concentration
14. Negative free water clearance: SIADH
15. Regarding DCT which of the following is correct? =Site of action of thiazide Diuretics
16. BP 160/110 mmHg & increase renin is due to: =sympathetic Renal nerve
17. Edema/Ascites in liver patient is due to: =Decrease Oncotic Pressure
18. Substance having more properties than inulin is thought to have = Inc filtration rate and net secretion
19. Renin is persistently increased in = secondary essential HTN > malignant essential HTN
20. Is summer fasting man, have concentrated urine due to = Increase ADH
21. An 8-year-old patient was present to the Clinic with periorbital edema. His labs showed protein greater than 3.5g/dl, What is the probable cause = Albuminuria and sodium retention
22. After sweating which of the following electrolytes maintain homeostasis = Sodium
23. Which of the following is found more in ICF as compared to ECF = Potassium
24. After RTA due to hemorrhage a person with 2 liter blood loss, the blood volume restored back by: = DCT
25. After marathon race a person lost 2 liters of sweating he drinks 2 liters of water what will happen? = Decrease Osmolarity of ECF. (prefer inc ICF volume if given in options in exam).
26. In dialysis patient accurate Clinical way of monitoring of GFR is: = Creatinine Clearance
27. RBC is kept in hypertonic solution containing Urea what will be the result? = Shrink, Swell & lyse
28. Patient presented with decrease BP. Which one of the following will secrete enzymes to normalize the BP of patient = JG Cells
29. ECF is different from ICF in: = Inorganic ions
30. After RTA, patient came with excessive bleeding, Cause of decrease GFR is: = Decrease Arterial blood flow
31. Absorption of HCO_3^- occurs in = PCT+CD
32. Difference between ICF and ECF? = Less PH of ICF. Difference b/w ECF & ICF is = Inorganic ions
33. Free water clearance regulated by = ADH
34. A patient with urine osmolarity 1200 Serum osmolarity 220 what is the cause? =SIADH
35. A patient having CO_2 583 PH 7.3 and HCO_3^- 24 which type of acid base balance? =Respiratory Acidosis
36. Erythropoietin is stimulated by =Hypoxia
37. Renal correction of hyperkalemia lead to = Acidosis
38. Kidney activates which of the following =Cholecalciferol (1 alpha hydroxylation of Vit D3)
39. A patient of asthma having followed ABGs PH 7.23, HCO_3^- 26 and Hypercapnia likely acid base disorder is: = Respiratory acidosis (PH is acidic, Hypercapnia- CO_2 raised – so, a Respiratory disorder)
40. Action of aldosterone = cytoplasmic receptor, displaces Na channels from cytoplasm to cell membrane
41. A patient with severe diarrhea what infusion will be given to increase ECF and decrease ICF causing plasma expansion after osmotic equilibrium = 1 Liter of 3 percent NaCl
42. Vasopressin secretion is increased by: =Decreased pressure in the right ventricle
43. A patient ABGs reveals PH 7.54, PCO_2 40 and HCO_3^- 29 what is acid base disorder? =Uncompensated Metabolic alkalosis (PH is alkaline 7.54, Pco_2 normal, HCO_3^- raised- indicates metabolic disorder)
44. Ammonia is urinary buffer because: =Impermeable to absorb NH_4^+
45. Diagnostic findings of metabolic alkalosis are = $\text{HCO}_3^- > 24$

46. Plasma clearance of PAH is used to measure the renal plasma flow because it = Is filtered and secreted but not reabsorbed
47. Which of the following hormones regulates osmolarity = ADH
48. Which part of nephron is impermeable to water = Thick Ascending loop of Henley
49. The basic function of kidney is = Metabolic waste removal
50. Surgeon more curious about which electrolyte before surgery on serum electrolytes report = Hyperkalemia
51. Prolong diarrhea will result in = Metabolic alkalosis
52. Systolic pressure is highest in which of the following vessel = Renal artery
53. A person loses 2L OF sweat while working and drinks 2L pure water what change will occur = Inc ICF vol
54. Increase sodium uptake in body is due to: = Increase K⁺ in body
55. Hypotonic fluid is present in which part = Early DCT
56. A man was taken to the high altitude where after 10 days patient ABG's sample taken which of the condition ABG's show: = Metabolic acidosis
 - i. Explanation: acute respiratory alkalosis compensated by Met acidosis in 10 days
57. Thirst increased by: = Increase Angiotensin 2
58. To calculate plasma osmolality, sodium concentration is multiplied with 2 because of = Anions
59. Which condition leads to hypokalaemia? = Increase PH
60. Fluid of choice for third space fluid loss? = Ringer lactate
61. Highest systolic pressure is seen in which of the following? = Renal artery
62. Best indicator of dialysis: = Creatinine clearance
63. Patient with CO₂ 44, PH 7.3, HCO₃ 16 what is the acid- base abnormality? = Metabolic acidosis
64. Which of the following decrease the arterial oxygen saturation without decreasing arterial O₂ tension = CO poisoning (PaO₂ remain normal in CO poisoning ☐ anemic hypoxia)
65. Which one decreases plasma osmolarity = ADH
66. Erythropoiesis is mainly stimulated by = Erythropoietin.
67. Plasma oncotic Pressure majorly due to = Albumin
68. Formation of interstitial fluid increases with decrease: = plasma colloid osmotic pressure
69. Primary dehydration will have: = Increase ECF osmolarity
70. Which of the following decreases osmolarity? = Vasopressin (ADH)
71. What is the most appropriate test for urine culture = CLED agar with 1ml urine
72. Which of the following factors increases GFR? = Afferent arteriolar dilation
73. Glomerulus is formed by: = Afferent arteriole
74. Aldosterone Act mainly on: = CCD
75. Increases GFR due to increase: = Hydrostatic pressure
76. GFR is measured by Inulin. Volume of plasma Filter per unit time: = GFR. Normal GFR = 125ml/min
77. Angiotensin 2 shortest function: Arteriolar vasoconstriction
78. Regarding distal convoluted tubule: = Confers final composition of urine
79. By increasing specific gravity of urine which functions is test? = Concentration
80. A young patient presented with high glucose Kassmaul breathing and unconscious and urinary ketones positive and Diagnose of DKA made which one act as buffer in this condition = HCO₃
81. What changes are seen in a patient who is given 1L of N/saline = increased urine osmolarity
82. Hyperkalemia is associated with: = Acidosis
83. In severe dehydration the following changes occur: = ECF become hypertonic
84. Sodium levels in body are regulated by: = Aldosterone
85. PAH is used to measure: = Renal plasma flow
86. Minimum amount of urine should be excreted per day to pass metabolic waste: = 500ml
87. Lymph flow decreased by increase of: = Increased oncotic pressure
88. In chronic respiratory acidosis what is normal? = PH of plasma
89. Ureteric obstruction causes: = Decreased GFR
90. In summer, fasting man, have concatenated urine due to: Increase ADH
91. Angiotensin 1 conversion occurs in = lung. Activated in lungs = AT 2
92. Counter current exchange mechanism occurs in = presence of vasa recta
93. Counter current multiplier = Loop of Henle and JG cells
94. Main action of aldosterone: = Maintenance of Na & K in body fluid

95. Amount of substances filtered per minute minus the amount of substances that appears in urine: Tubular reabsorption
96. Difference between tubular fluid of PCT and DCT is =Increased in H^+ secretion in DCT as compared to PCT
97. In syndrome of apparent mineralocorticoid excess (AME) what will be present? =Hypertension
98. Dehydrated patient which ion immediately help in compensation? =Na
99. Primary adrenal insufficiency will cause: =Hyperkalemia
100. Fenestrated capillaries in =Kidney
101. Urinary output in 70 Kg man is =1.5L
102. Dehydration which affected not = PCT (ischemia affects PCT first)
103. RBC swell when placed in? = Urea 250mmol
104. Action potential reduced in: =Hyponatremia
105. Sodium absorption function of: =Aldosterone
106. A man smoker having hyponatremia and hyperosmotic urine most likely have: =Inappropriate ADH syndrome
107. Negative water clearance is due to: =Increase ADH
108. Kidney best mechanism to preserve volume: =Renin secretion
109. PH is defined as: =Negative log of H
110. In metabolic acidosis how is compensation done: =Increase glutamine secretion
111. What is the role of ECF =Exchange of substances
112. Erythropoietin is released by which Organ = Kidney
113. Imp mechanism for Tubuloglomerular feedback = decrease peritubular Na concentration
114. Pt passing dilute urine, problem with Tubuloglomerular feedback, what other factor you will see = Low urinary sodium conc.
115. Regarding myogenic vascular response → vasoconstriction in response to inc B.P.
116. Decrease Lymphatic flow due to: =Hemorrhage
117. A patient of asthma has PH 7.23, HCO_3^- 26 and hypercapnia likely acid base disorder is =Respiratory acidosis
118. ADH causes which effect = Increase urine osmolarity
119. 3 weeks old child with h/o projectile vomiting since birth findings will be = Hypochloremic metabolic alkalosis
120. A patient of burn given Succinylcholine after which ECG shows tall T wave due to pharma = Hyperkalemia
121. Metabolic acidosis is due to = Decrease Bicarbonate in blood
122. ABG's of a patient show PH:7.3 HCO_3^- 15 PCO_2 : 38 diagnosis = Metabolic acidosis
123. What is common feature of primary adrenal insufficiency = Hyperkalemia
124. Known patient of CKD taking dialysis twice a week how will you decide between transplant and to continue dialysis = Creatinine clearance
125. Known CCF patient developed pedal edema and pleural effusion pleural tap done what will be findings of fluid suggestive of transudate = Low cell count
126. Female at gestational age 34 having symphysio fundal height of 28 weeks cause may be = Renal agenesis
127. Patient present with low serum calcium and ionized calcium, high serum phosphate, increased PTH, most likely suffering from = CRF
128. Horseshoe kidney associated with = plevi ureteric junction abnormality
129. A patient is suffering from chronic renal failure and on dialysis. Increase in which parameter of blood is alarming to doctor = Potassium
130. A male patient presented with history of fever, significant weight loss, painful micturition, hematuria and having raised creatinine and hematocrit. He is having cancer of which of the following organ = Kidney
131. An I/V urograph of 8 year old child shows fusion of lower poles of kidney which one of the following is most likely condition = Horse shoe kidney
132. In hemorrhage patient aldosterone level increased by: =AG2
133. Minor calyx receives urine from: =Papilla
134. Malignant hyperthermia occurs due to changes in which of the following? =Calcium
135. Hyperkalemia is caused by: =Exercise
136. Aldosterone exerts its maximum effect on which of the following site? =CCT
137. PH = 7.49 PCO_2 = 60 HCO_3^- = 30 which of the following Acid Base abnormality does it indicate? =Partially compensated respiratory acidosis
138. Main determinant of plasma osmolarity is = Sodium. Effect of hypernatremia on the body = Cell shrinkage

139. Which of the following decreases osmolarity = Vasopressin (ADH)
140. Albumin & RBCs in urine due to damage of: = Glomerulus
141. Which of the following is a prominent feature of RTA 4 = Hyperkalemia
142. Which of the following drug is actively secreted by kidneys = Penicillin
143. If ICF is increased what will decrease? = Heart rate
144. After sweating which of the following electrolyte maintain homeostasis: = Sodium
145. Lady after hemorrhage goes into Acute Kidney injury -- part of nephron will be most likely affected = PCT
146. Protein can't cross GMB due to = negative charge
147. Which of the following is urine output in a 70kg person in 24 hours? = 1500ml
148. Afferent Renal arterioles from = Glomerulus
149. Which of the following ion has profound effects in ECF = Sodium
150. The ability of the kidney to excrete concentrated urine will increase if: = The rate of blood flow through the medulla decreases
151. Which of the following is the function of Erythropoietin? = Increase Hemoglobin
152. Renin is inhibited by = AT II
153. Hemoglobin saturation increases in which of the following conditions? = Increase PO₂
154. A person drinks 600 ml of water how much water of it will be present in plasma: = 50 mL
155. Patient having signs of hypoxia with normal breathing PO₂ 95, PCO₂ 24 and HCO₃, 18 with normal PH: = Fully Compensated Metabolic Acidosis
156. Which of the following has same osmolarity to plasma = 0.9 % N/S
157. A 60 years old businessman is evaluated by physician for his high BP which was 185/130mm Hg, Lab revealed increased plasma renin activity. His plasma aldosterone level is high, Left renal vein Renin level is high and right Renal vein Renin Level is decreased, Most likely diagnosis is = Left renal Artery Stenosis
158. Mesangial cells have contractile property which helps them to maintain = Renal blood flow
159. Fanconi syndrome, decrease ATP at the PCT linked with: = Glycosuria
160. Most potent stimulus for release of aldosterone is: Hyperkalemia
161. Which of the following cause vasoconstriction? ADH
162. Which of the following substances can be used to measure the volume of plasma? = Even blue dye
163. Hyponatremia may be due to = Inc H₂O level (dilutional hyponatremia)
164. The part of nephron that amounts for 60-80% water absorption: = PCT
165. Concentration of a substance in urine is 2 moles/L. Urine flow rate is 100 m/s and plasma flow rate is 10 m/s. How much substance will be cleared? = 20
166. An 8 years old patient present to the clinic with periorbital edema. His labs showed protein greater than 305g/dl. What is the probable cause? = Albuminuria and sodium retention
167. The PH of urine can't be lowered below 5.4 even after giving Bicarbonates (HCO₃). What is the condition termed as? = RTA 1
168. Micturition is controlled by: = Mechanoreceptors in bladder wall
169. Low depolarization occurs in: = Hyponatremia
170. ECF volume increases maximum on giving: = Hypertonic saline
171. The slope pertaining to the action potential changes with: = Hyponatremia
172. Severe diarrhea leads to: = Metabolic acidosis with normal anion gap
173. Plasma colloid oncotic pressure is maintained by: = Albumin
174. The network of arteries inside glomerulus: = Tuft of Capillaries
175. 0.5 g/dl protein is present in which fluid = Lymph
176. Proliferation of renal system: = Mesangium
177. An increase in the concentration of plasma potassium causes increase in: = Secretion of aldosterone
178. Patient brought in shock in emergency department. Successful fluid replacement will be indicated by = Increase in urine output
179. A patient is suffering from severe Diarrhea K⁺ infusion given K⁺ go into cell through which = Na-k pump
180. A man drink 2L of water to replenish the fluids lost by sweating during a period of exercise. Compared with the situation prior to the period of sweating: = His intracellular fluid volume will be greater
181. Diabetic patient has increase urine and frequency due to? = Decrease glucose absorption
182. In hypertensive patient what is cause of edema? = Increase Hydrostatic pressure
183. Potassium depletion may cause: = Rise in plasma bicarbonate
184. Hyperaldosteronism associated with all except: = Metabolic acidosis

185. In burn patient succinylcholine isn't given due to which of the following effect: =Hyperkalemia
186. Kidney changes in hypovolemic shock include = Acute tubular necrosis
187. Renal capillary filtration = Decrease with dehydration
188. Serum sodium is regulated by = Osmoreceptors
189. Highest sodium channel concentration in = Node of Ranvier
190. Na is major ECF cation. It is mostly balanced by which anion = Cl
191. More in dialyzing fluid as compared to plasma = Glucose & HCO₃
192. 0.85 % saline contain how much NaCl = 850 mg / 100 mL
193. Maximum renal T_{max} is for = Glucose > lactate
194. Proteins doesn't appear in urine because of: =Basement membrane
195. In severe dehydration: =Whole body fluid will be low
196. A patient with COPD and PO₂ 55, HCO₃ 26, pCO₂ 49 and PH 7.3: =Type II Respiratory failure with uncompensated Respiratory Acidosis
197. Intracellular buffer: =Protein
198. A middle-aged man come back from Cairo & developed painless hematuria likely diagnosis is= Squamous cell carcinoma of the urinary bladder
199. Patient presented with complains of cough and hemoptysis kidney biopsy how granular deposition of antigenantibody complex with C1Q is positive and GBM splitting noted this is related to =Membranoproliferative GN
200. Child is having proteinuria flank pain which protein deficient in this case=Albumin
201. In uremic nephropathy there is what type of anemia occur=Normochromic Normocytic anemia
202. A man presented with fever, rigors & and pus in urine which is treated for 2 weeks is most likely suffering from=Acute Pyelonephritis
203. A 7 years old school going boy develops sore throat. He received antibiotic for it, which resolved it, following 2weeks later, he developed generalized body edema, hypertension, and hematuria type of hypersensitivity =Type 3
204. Type 2 diabetes patient has weakness and increase frequency of urine since 2 weeks. What is possible mechanism of polyuria= Decreased glucose reabsorption from PCT
205. Patient presented with complain of fatigue, cough with hemoptysis and hematuria for 2days. Renal biopsy glomerulonephritis with linear deposits of IgG along the GBM. what is the likely cause=Good pasture syndrome
206. ADH is inhibited by: =Alcohol
207. Which ion is passively absorbed renal tubules =Cl
208. Contraction of smooth muscles by: =Antidiuretic hormone
209. What are present in the thin loop of Henley? =Flat epithelium
210. Urine flow rate 1ml/min lowest osmolarity in which part? =DCT
211. For a substance X GFR 125mg/ml, T_m 125mg / min, plasma concentration is 200mg/100ml, what will be the filtration, reabsorption, and excretion of substance X? =250 filtration, 125 reabsorptions and 125 excretions
212. Formation of interstitial fluid increases with decreased in =Plasma colloid osmotic pressure
213. Zinc is important essential element one the following: = Carbonic anhydrase
214. Carbonic anhydrase is present in = membrane of RBCs
215. Renin is inhibited by: = Vasopressin (ADH)
216. Which of the following statements is unlikely to be true about H⁺ in the renal tubules? =it can bind with NH₄⁺
217. Inhibitors of carbonic anhydrase will cause: =Acidosis
218. Which of the following substance is more concentrated at the end of proximal convoluted tubule as compared to beginning of proximal tubules? =Creatinine
219. Composition of normal saline = 9g NaCl in 1000 mL distilled water
220. **How** to differentiate between normal in SIADH: =Plasma osmolarity
221. Patient has oat cell carcinoma secreting ADH. What he will have =Hyperosmotic over hydration
222. Respiratory acidosis cause is: = Barbiturate poisoning
223. Patient with severe dehydration how much minimum urine output daily to eliminate nitrogenous waste product from body: =400 to 600ml
224. Cause of raised anion gap: =DKA
225. Insensible water loss from skin in moderate climate: =200-400
226. Product of GFR and plasma concentration of substance: =Filtration Load

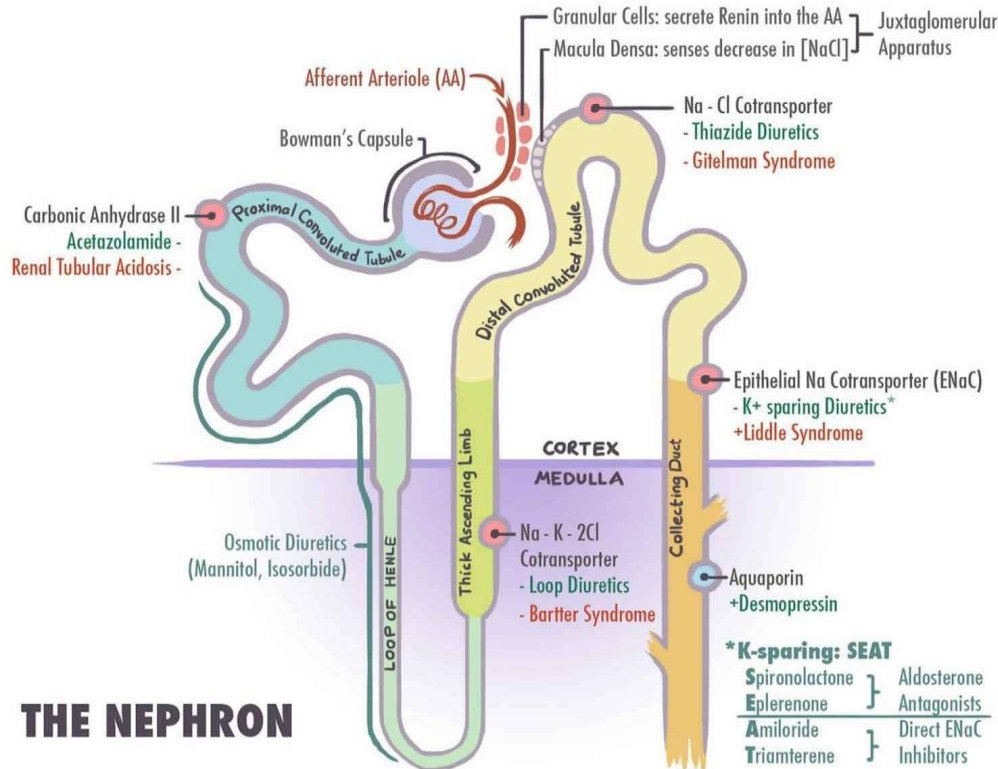
227. Renal threshold for glucose: =200
228. Which extracellular fluid increase level can cause more effects on heart? =K⁺
229. TBW in infants = 80%
230. Best way to measure high protein levels in plasma: = Urinary nitrogen content
231. Patient had prolonged vomiting. Metabolic alkalosis in patient is caused by: =Decreased Hydrogen
232. Infusion of 140meq sodium in 100ml water causes: = Increased osmolarity both ICF and ECF
233. Patient has chronic respiratory acidosis. For every 10 rise in pCO₂ the compensatory rise in HCO₃ is = 4
234. Patient presented with excessive diarrhea and vomiting. Dx Metabolic Alkalosis is made =when Hco₃ >25
235. Regarding Function of lymphatic's: =Take plasma fluid back to body
236. A Patient of chronic nephritis, presented with anemia. What is to give this patient as treatment -- Erythropoietin
237. A patient presented with severe metabolic alkalosis BP was 190/110 (hypertension) and serum potassium was 1.9 there is increased aldosterone level in his blood: =Primary Hyperaldosteronism
238. A 45-years old man fell from roof top presented with Head injury and hyperventilation His Arterial blood gases shows PH 7.134, Po₂ 25 Hco₃ 19 his CT report was normal, What is wrong with this patient? =Metabolic acidosis
239. Gitelman's syndrome is defect in which part of kidney = DCT
240. Cause of metabolic alkalosis is = Loop diuretics
241. High serum concentration of potassium causes: = Peaked T waves
242. 237 answer miss Low serum concentration of calcium causes:
243. HCO₃ is absorbed at which of the following site = PCT+ CT
244. Substance having more properties than inulin is thought to have =Increase filtration rate and net secretion
245. Which Part of nephron is impermeable to water = Thick ascending loop of Henley
246. Which of the following causes increase in renin level = Decrease stretch on cardiac receptor
247. ADH decrease sodium level Hyponatremia is caused by (Med. Feb.) = Increase water intake
248. Patient came with generalized edema. Urine examination reveal Proteinuria cause =Hypoalbuminemia
249. Thirst is increased by =Increase Angiotensin 2
250. How much urine should be made to match the osmolarity of 570 when normal is 1440? = 0.25
251. A young patient blood pressure is 150/95 his serum renin is higher than normal which of the following the stimulus for this increase level of renin is =Sympathetic stimulation via renal nerve
252. Voluntary inhibition of micturition reflex is by activation of =Pudendal nerve
253. Primary dehydration will have =Increase ECF osmolarity
254. A patient present with BP of 180/110 due to Release of Renin Which of the following kidney structure is involved =JG Cells
255. Increase production of concentrated urine is due to (Med. Feb.) =Increase Permeability through CD
256. What is immediate and shortest action of angiotensin 2 =Vasoconstriction
257. Renal plasma flow is measured by =paraamino hippuric acid (PAH)
258. Child with generalized body edema cause is =Hyperproteinemia
259. Strongest stimuli for erythropoietin are =Hypoxia
260. In Nephrogenic diabetes, what will occur =ECF osmolarity increase
261. Regarding histology of normal left kidney =Podocyte on visceral layer of bowman capsule
262. Most common nephritic syndrome in adult: = IgA nephropathy
263. Most common nephrotic syndrome in infants: =Minimal change disease
264. The association of IgA nephropathy is which kind of deposits=Meningeal deposits
265. Most common nephritic syndrome in adult=IgA nephropathy
266. Most common nephrotic syndrome in infants=Minimal change disease
267. Which one is nephrotic syndrome=Amyloidosis
268. RBC cast seen in=Glomerulonephritis
269. A lady CRF, blood sample taken and put into refrigerator, in next morning results are, Sodium 140, K 6, LDH600, creatinine raise, this is due to=Hemolytic reaction of blood sample
270. A 11-year-old boy faced abdominal trauma and then presented to emergency. On labs there was 1+ blood and 3+ protein in Urine. What is the pattern of inheritance
271. 46 years male presented with nephrotic syndrome Immunofluorescence microscope of renal biopsy showed Sclerosis with deposition of IgM and C3. Likely diagnosis= Focal segmental glomerulosclerosis

272. Adult polycystic kidney disease of transmission is= Autosomal dominant
273. A middle age known ESRD list for hemodialysis multiple transfusion done Normocytic normochromic anemia which is more appropriate therapy= S/C erythropoietin
274. A 70 years old with recurrent UTI most likely due to= Outflow obstruction
275. A 60 year old businessman is evaluated by physician for his high BP which was 185/130mm Hg. Lab revealed increased plasma renin activity. His plasma aldosterone level is high and right renal vein renin level is decreased . Most likely diagnosis is =Left renal artery stenosis
276. A boy with H/O of pharyngitis having Raised ASO high amount proteinuria mechanism of disease=Antigen antibody complexes in different tissue
277. Renal tubular necrosis would result in which of the following = Hyperkalemia
278. A children with generalized edema on urine examination proteinuria 2+ there is GBM thickening what type of deposit will be seen=Sub Epithelial
279. Granulomatous lesion in bladder, after few years progressed to carcinoma this is caused by=Schistosomiasis
280. A 70 kg man has cholesterol level of 200, creatinine 0.8, BUN 20, Proteinuria of 30mg/dl, glycosuria ++, fasting blood glucose 88, and hypertension cause of this hypertension is = Glomerulonephritis
281. Patient presented with loin pain and mass in pelvis with hematuria suspected carcinoma is= RCC
282. A lady on antihypertensive collapsed with serum potassium 6.7 and other signs, is due to= acute Renal failure
283. A patient with labs showing decreased calcium level increased phosphate level and increased PTH is a case of=CRF
284. A known patient of MI with pericardial friction rub having raised creatinine and urea most likely complication is= Uremic pericarditis
285. Patient is passing dilute urine (asthenuria), there is Tubuloglomerular concentrating problem, what other factor you will see in this condition=Low urinary sodium
286. A patient has severe hypovolemia which kidney changes will be prominent=Acute tubular necrosis
287. Patient presents with pain in lumbar region. Stone at pelviureteric junction pain arising from which segment = T12 – L2
288. Which of the following tumor is of embryonic origin in infancy=Nephroblastoma
289. A child having tumor with blue cells which is secreting catecholamines and is because of gene amplification which is the most probable diagnosis= Neuroblastoma
290. Crescents are mainly formed by=Parietal cell with increase Neutrophils
291. A male patient presented with history of fever, significant weight loss, painful micturition, hematuria and having raised creatinine and hematocrit. He is having cancer of = Kidney
292. Patient with history of multiple myeloma now has hypercalcemia, polyuria and confusion urine osmolality is 310 mosm/1, what is the reason of polyuria= ADH can't act on tubules
293. A young boy after strenuous exercise felt pain in lumbar region. History of stone what is suitable investigation to reach diagnose=Ultrasound KUB + CT KUB
294. Sympathetic nerve block to urinary bladder will cause which of the following = Pain and filling sensation loss
295. A 4p year old man come in ER with complain of body weakness and oliguria he gave history of taking some drug for weight gain from general quack urine detailed report urine specific gravity is 1.010 urea creatinine is raised ALT urine calcium is raised the likely diagnosis is =Nephrocalcinosis
296. Edema in nephrotic syndrome is due to=Hypoalbuminemia
297. Patient went through cystoscopy due to hematuria. Later developed fever and hypotension cause of hypotension= Sepsis
298. Hypokalemic metabolic alkalosis leading to volume expansion is seen in= Conn syndrome
299. A lady with persistent diluted urine likely cause explaining defect in tubular concentration mechanism=Decrease urine sodium
300. BUN/Cr ratio greater than 20 cause will be=Pre renal azotemia
301. Low calcium high phosphate no increase in CAMP on giving PTH likely due to=CRF
302. IgA Nephropathy deposits are=Mesangial
303. Patient met an accident and was brought to emergency department. BP 80/40, Tachycardia, Low urinary output after catheterization. Renin was increased due to=Decrease in arterial blood flow

304. Vitamin D resistant rickets occurs in = Fanconi syndrome
305. In nephrotic syndrome edema is due to = Decrease oncotic pressure
306. Crescents in glomeruli are formed due to proliferation of = Parietal cells
307. Diagnostic test for diabetic nephropathy is = Microalbuminuria
308. Decision between dialysis and transplant is by = Creatinine clearance
309. On electron microscopy, PSGN shows = Sub epithelial deposits
310. On immunofluorescence, IgA nephropathy shows = Increased mesangial deposition
311. 5 years old girl is brought to the physician because of facial swellings, puffy eyes and swollen legs, she had history of mild cellulitis after a mosquito bite 3 weeks ago, and her urine sample shows a reddish brown hue and contains both RBCs and proteins. Which of the following will most likely be seen on renal biopsy = Sub epithelial electron dense hump
312. Selective proteinuria occurs in = Minimal change disease
313. In crescentic glomerulonephritis antibody complex deposition on GBM which type of hypersensitivity = Type 2
314. Carcinoma that is associated with increased hemoglobin = Renal cell carcinoma
315. Man with history of being not well for long time Hb was 17 and on ultrasound there is 3 or 6 cm spherical mass found on lower pole of kidney diagnosis is = Renal Carcinoma
316. CKD with low calcium cause is = Decrease 1, 25 Dihydroxycholecalciferol
317. Pregnant lady of 12 weeks gestational amenorrhea presented with rigors and chills high grade fever due to = Acute pyelonephritis
318. A patient has fever of 40°C with flank pain increased frequency chills and rigors. Diagnosis is done by = Blood and urine culture
319. The imbalance in hemostasis in case of uremia due to = Platelet function defect
320. Fanconi syndrome a rare genetic disorder. The child will present with = Glycosuria
321. 59 year old patient known case of CRF presents with anemia due to = Erythropoietin deficiency
322. Patient presented with periorbital edema and proteinuria and RBCs cast on urinalysis, the problem is in = GBM
323. Benign tumor among the given is = Warthin tumor
324. A child X-Rays showing unilateral hydronephrosis. What is the cause behind this = Pelvic ureteric junction obstruction
325. Which one rises significantly in end stage renal disease = Creatinine
326. A day following hysterectomy, a patient complains of severe pain in the right upper lumbar region of the back. Which of the following structures was most likely damaged during the surgery = Ureter
327. I/V urography of 8-year-old boy shows normal right kidney but shows absence of kidney on left side and small shadow appears in pelvic region cause is = Pelvic kidney
328. Site of impaction of ureteric stone = Opening of ureter into bladder
329. Which of the following is paraneoplastic syndrome of kidney = Polycythemia
330. Clear cells on histology organ is = Kidney
331. A sample of blood was drawn from the vein of a patient of renal failure, which of the following is estimated from this sample = Creatinine
332. A 60 years old male presented with history of fever, significant weight loss, painful micturition, hematuria, and flank mass, his Hb is 18 what could be the possible pathology associated with his condition = Renal cell carcinoma
333. ASO-Titer is used as marker for = PSGN
334. Which of the following is the action of Oxytocin = Ejection of milk
335. Patient having hypokalemia, hypertension, with normal cortisol & VMA & raised aldosterone is most likely suffering from = Conn's Syndrome
336. A known case of CRF, likely gland to enlarge = Parathyroid
337. A patient with hematuria and RBC cast in urine. Structure involved = Glomerulus
338. Good pasture syndrome related to = Linear deposition
339. A renal disease with continuous elevated levels of renin = Adult polycystic kidney disease
340. The renal problem associated with SLE = Lupus Nephritis
341. A patient presents to the clinic with polyuria, polydipsia, and urine Osmolality of 310 mOsm, he is a case of multiple myeloma, what is the cause of polyuria in him = Renal tubules do not respond to ADH

342. True regarding kidney = Podocytes in visceral layer of Bowman's capsule
343. An old age diabetic lady with CRF is on dialysis. Her X-ray lower limb, femur head shows loss of trabecular bone. Which hormone is responsible for such X-ray findings = PTH
344. 20 Years old patient presented with increase urea, creatinine & increase K⁺ level = AKI
345. A patient is suffering from chronic renal failure and on dialysis. Increase in which parameter of blood is alarming = Potassium
346. An old lady presented in medical emergency in unconscious state. Her Bp 180/90, Temp 39, pulse 90. Labs are Glucose 350mg/dl Na 130, K 3.5, Urea is 10. Diagnosis = Chronic Renal failure
347. In post streptococcal glomerulonephritis finding is = Sub epithelial deposits
348. 24, 25 dihydroxycholecalciferol increase in = Chronic renal failure
349. Hypercalcemia and renal failure. Cause = PTH adenoma
350. A patient with epistaxis, hematuria, saddle nose & granulomatous inflammation diagnosis is = Wegner granulomatosis
351. Young patient developed ARF after PPH which part of kidney is most likely damaged = PCT
352. Main cause of edema in nephrotic syndrome = Hypoalbuminemia
353. Patient with renal artery stenosis may present with very high blood pressure due to increased renin secretion. Which of the following structure in kidney responsible for sensing inadequate perfusion and secreting renin = Efferent Arterioles
354. Adrenal insufficiency main feature = hyperkalemia
355. Edema due to renal cause can be due to = Na retention and albuminuria
356. Retic count decrease in = Chronic renal disease
357. Child with generalized edema and proteinuria 6g per day. Which part of the kidney involved = Basement membrane
358. Proteins normally don't leak out in tubular fluid due to = Basement membrane is negatively charged
359. A person who returned from a trip in Cairo presented with painless hematuria. Which type of cancer has he developed = Squamous cell carcinoma
360. Rectal biopsy was done. How to diagnose ameba infection = PAS
361. Type 2 tubular acidosis is due to = Defect in HCO₃ reabsorption
362. There is increased risk of carcinoma of bladder exposure to = Aryl Amines
363. Focal segmental Glomerulosclerosis = Subepithelial humps
364. Long standing HTN... now shortness of breath, edema is due to = Increased hydrostatic pressure
365. An i/v urograph of 8 year old boy shows normal kidney on right side but absence of shadow appear above the bladder on left side which of the following is the condition = Left pelvic kidney
366. IgA nephropathy is associated to = Berger disease
367. Calcium stones formation may be prevented by which process = Complex formation
368. Congenital erythropoietin porphyria. What is finding in urine = increase urine uroporphyrin 1
369. A lady with CRF patient, sample taken which was placed in refrigerator over night, next day, normal sodium, raised k(6.3) raised PO₄ and LDH(600) what is the cause = Hemolysis of blood sample
370. A 35 year female having malar rash and positive anti ds DNA now develops proteinuria & hematuria the most likely cause will be = Lupus nephritis
371. Addison's disease patient present in which emergency condition = Coma
372. Granulomatous lesion in bladder, after few years progressed to carcinoma this is caused by = Schistosomiasis
373. Pregnant lady of 12 weeks gestational amenorrhea presented with rigors and chills high grade fever due to = Acute pyelonephritis
374. In Cushing syndrome following occur = Eosinopenia, lymphopenia, neutrophilia
375. An old patient presented with fatigue weakness and dyspnea with labs showing decreased calcium level, increased phosphate level, raised creatinine and increased PTH is a case of = ESRD
376. Smell of Burnt urine is present in = Maple Syrup urine disease
377. Diagnostic findings of metabolic alkalosis are = HCO₃>24
378. A man is a plumber he is having difficulty in breathing from last 1 year he is also short of breath and dyspnea his blood ABGs show PH 7.4 HCO₃ 19 and PVO₂ 31 he has most likely = Compensated metabolic acidosis

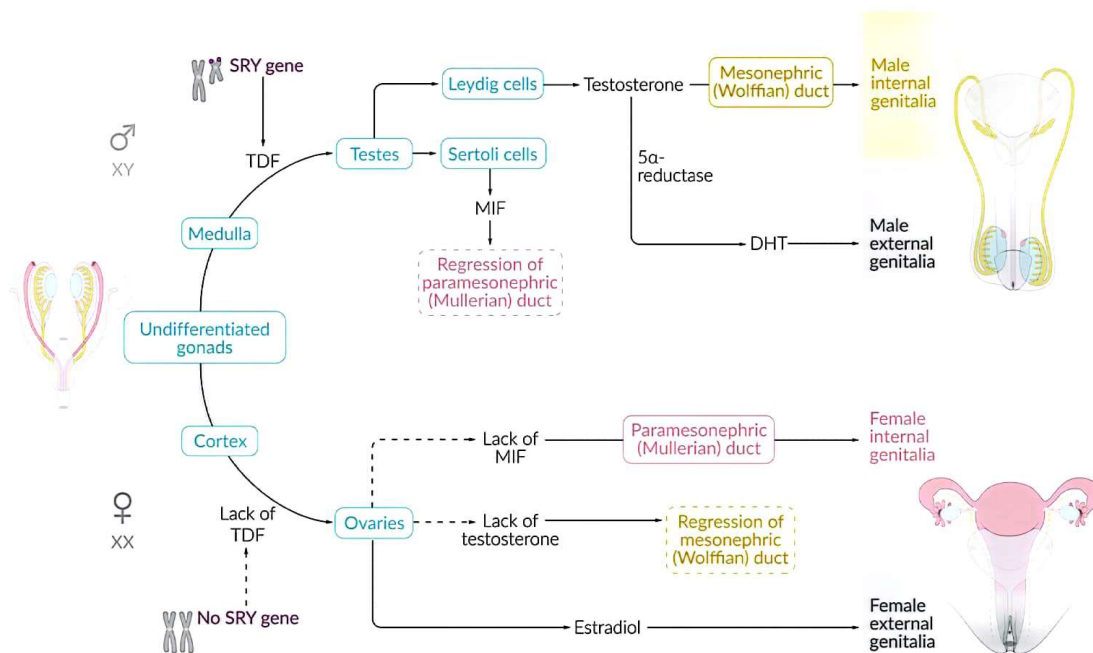
379. A patient presented with severe diarrhea and vomiting. He ABGs are PH 7.23 HCO₃ 16 and PCO₂ 36 he is having = Metabolic acidosis
380. A female having low calcium high PTH and parathyroid hyperplasia due to = CRF
381. A patient came to you with hematuria what is the level of injury = Glomeruli
382. Patient has hematuria, hemoptysis on microscopy glomerular linear deposits seen what is diagnose = Goodpasture syndrome
383. A patient has following ABGs PH of 7.2, HCO₃ levels of 19 and PO₂ OF 39 what is likely diagnose is = Metabolic acidosis
384. A 70 kg man has cholesterol level of 200, creatinine 0.8, BUN 20, Proteinuria of 3mg/dl, glycosuria ++, fasting blood glucose 88, and hypertension cause of this hypertension is = Glomerulonephritis
385. I/V Urography of 8 year old boy shows normal right kidney but shows absent of kidney on left side and small shadow appears in pelvic region cause is = Pelvic kidney
386. Drug leading to hyponatremia in SIADH pharma = Carbamazepine
387. Patient presented with history of head trauma his urine osmolarity was decreased & plasma osmolarity also increased, polyuria and positive CH₂O clearance, likely cause would be = Central Diabetes insipidus
388. Buffer found in kidney but not in plasma: = Ammonia
389. Max absorption of glucose occurs from: = PCT
390. Decrease in nerve action potential excitability of RMP is due to: = Hypocalcemia
391. Most abundant blood buffer is which of the following. = HCO₃
392. GFR increase by which of following = decrease plasma colloid osmotic pressure
393. Blood flow of renal system is regulated by which of following? = Tubulo glomerular feedback
394. Renal plasma flow decrease by: = Renal artery constriction
395. Which hormone works on the kidney? = Aldosterone
396. Na = 135, HCO₃ = 100, Cl = 5 calculate the anion gap: = 30
397. AG = Na - (Cl + HCO₃)
398. Hyperkalemia leads to = Flaccidity



REPRODUCTION

Differentiation of Sex – Basic concepts

- ❖ **Genetic sex** is defined by the sex chromosomes, XY in males and XX in females.
- ❖ **Gonadal sex** is defined by the presence of testes in males and ovaries in females.
- ❖ **Phenotypic sex** is defined by the characteristics of the internal and the external genitalia.
- ❖ **SRY gene on Y chromosomes is the testes determining factor (TDF)**
- ❖ **The testes of males secrete anti-mullerian hormone (AMH or MIF) and testosterone.**
- ❖ An imp. role of Sertoli cells is to secrete mullerian inhibiting factor or anti-mullerian hormone
- ❖ Testosterone stimulates the growth and differentiation of the wolffian ducts or mesonephric ducts, which develop into the male internal genitalia
- ❖ Anti-mullerian hormone (AMH) causes atrophy of the mullerian ducts (which would have become the female internal genital tract).
- ❖ The ovaries of gonadal females secrete estrogen, but not AMH or testosterone.
- ❖ Without anti-mullerian hormone, the mullerian ducts are not suppressed and therefore develop into the female internal genitalia

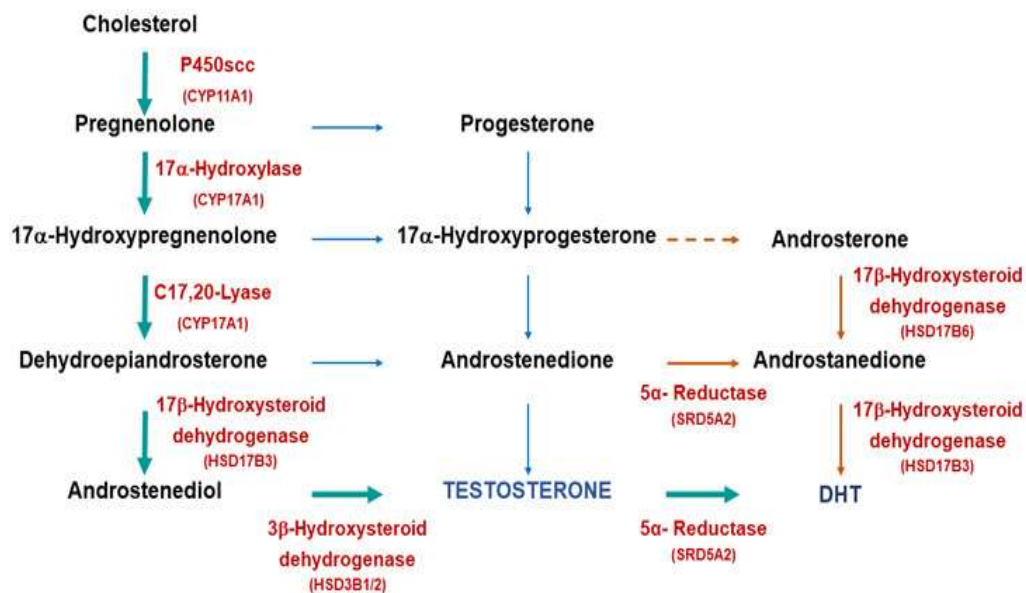


Key Facts:

- Leydig cells secrete testosterone → development of Male internal genitalia (Prostate, seminal vesicles, testis, epididymis, ejaculatory duct and accessory glands) via mesonephric/wolffian ducts
- 5 alpha reductase converts testosterone into dihydrotestosterone (DHT)
- **DHT causes the development of male external genitalia** (Penis and scrotum, prostate growth).
- Testosterone is the most potent anabolic hormone. **Potency of DHT is more than testosterone**
- Lack of AMH/MIF causes development of mullerian/paramesonephric duct into female internal genitalia. While, lack of testosterone causes regression of mesonephric duct
- Full development and functioning of seminiferous tubules require FSH and androgens

MALE REPRODUCTION

Testosterone synthesis	<ul style="list-style-type: none"> ❖ It is the major androgen synthesized and secreted by the Leydig cells. ❖ Leydig cells do not contain 21 α-hydroxylase or 11 β-hydroxylase (In contrast to the adrenal cortex) and, therefore, do not synthesize glucocorticoids or mineralocorticoids. ❖ LH (In a parallel action to ACTH In the adrenal cortex) Increases testosterone synthesis by stimulating cholesterol desmolase, the first step in the pathway. ❖ Accessory sex organs (e.g., prostate) contain 5α-reductase, which converts testosterone to its active form, dihydrotestosterone. ❖ 5α-reductase inhibitors (Finasteride) may be used to treat benign prostatic hyperplasia because they block the activation of testosterone to DHT in the prostate.
Regulation	<ul style="list-style-type: none"> ❖ Arcuate nuclei of the hypothalamus secrete GnRH into the hypothalamic-hypophyseal portal blood. GnRH stimulates the anterior pituitary to secrete FSH and LH. ❖ FSH acts on the Sertoli cells to maintain spermatogenesis. The Sertoli cells also secrete Inhibin B, which is involved in negative feedback of FSH secretion. ❖ LH acts on the Leydig cells to promote testosterone synthesis. Testosterone acts via an intratesticular paracrine mechanism to reinforce the spermatogenic effects of FSH in the Sertoli cells. ❖ Testosterone inhibits the secretion of LH by inhibiting the release of GnRH from the hypothalamus and by directly inhibiting the release of LH from the anterior pituitary. ❖ Inhibin produced by the Sertoli cells inhibits the secretion of FSH from the anterior pituitary. Inhibin is -Ve regulator of FSH ❖ In short, hypothalamic pituitary gonadal axis \rightarrow hypothalamic control by GnRH, anterior pituitary by FSH, LH and negative feedback control via testosterone and Inhibin.



Hormone	Functions
Testosterone	<ul style="list-style-type: none"> • Differentiation of epididymis, vas deferens, and seminal vesicles • Growth of penis and seminal vesicles, spermatogenesis, pubertal growth spurt • Inc in muscle mass, bone density and RBC production. Deepening of voice. libido • Closure of epiphyseal plate of bone. Levels are lowest in Pre-school age
DHT	<ul style="list-style-type: none"> • Differentiation of external genitalia (penis, scrotum) and growth of prostate • Male hair pattern and baldness. Activity of sebaceous gland (acne development)

Diseases of the Testes

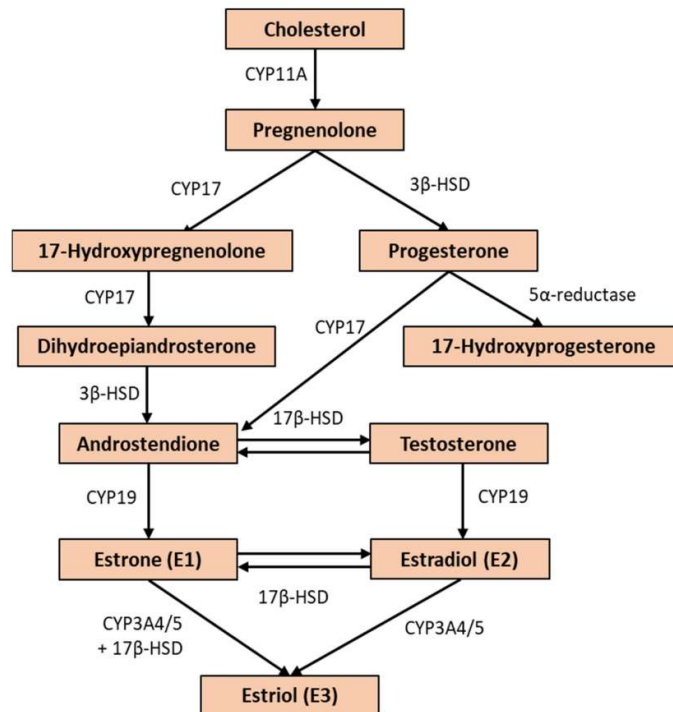
Cryptorchidism	<ul style="list-style-type: none"> ❖ Developmental failure of a testis descends into the scrotum. ❖ This condition is associated with increased incidence of germ cell tumors, especially seminoma and embryonal carcinoma. ❖ For cryptorchidism complication: Cancer > infertility
Hydrocele	<ul style="list-style-type: none"> ❖ It is serous fluid filling and distending the tunica vaginalis. ❖ Congenital hydrocele: due to incomplete obliteration of processus vaginalis ❖ Acquired hydrocele: secondary to infection or to lymphatic blockage by tumor. ❖ Transillumination positive
Varicocele	<ul style="list-style-type: none"> ❖ Dilated veins in pampiniform plexus due to venous pressure. ❖ Most often on left side because of ↑ resistance to flow from left gonadal vein drainage into left renal vein. Can cause infertility. ❖ Transillumination is negative ❖ On palpation- feels like bag of worms
Spermatocele	<ul style="list-style-type: none"> ❖ sperm-containing cyst. ❖ Due to dilated epididymal duct or rete testis

Testicular Tumors

<u>Germ cell tumors (GCTs 95%)</u>	
Seminoma	<ul style="list-style-type: none"> ❖ This tumor is analogous to dysgerminoma (tumor of the Ovary) ❖ It is the most common testicular germ cell tumor. ❖ Presents with Painless enlargement of the testis. ❖ Seminomas are extremely radiosensitive and can often be cured, even when there are metastases to abdominal lymph nodes. ❖ Excellent prognosis ❖ Findings: ↑ placental ALP, ↑ hCG. Fried egg appearance.
Embryonal carcinoma	<ul style="list-style-type: none"> ❖ This tumor is analogous to a similar tumor occurring in the Ovary. ❖ Early metastasis and worse prognosis than seminoma ❖ Findings : ↑ hCG levels
Yolk sac tumor (or) endodermal sinus tumor	<ul style="list-style-type: none"> ❖ This tumor is analogous to the endodermal sinus tumor of the Ovary. ❖ Most common testicular tumor in boys < 3 years old. ❖ ↑ AFP. The classic finding → Schiller-Duval bodies
Teratoma	<ul style="list-style-type: none"> ❖ This germ cell tumor is derived from two or more embryonic layers ❖ Malignant in adults. Benign in children
Choriocarcinoma	<ul style="list-style-type: none"> ❖ This tumor is analogous to Choriocarcinoma of the ovary. ❖ Histologically resemble placental syncytiotrophoblasts and cytotrophoblasts. ❖ ↑ hCG. Highly chemosensitive tumor
<u>Non-Germ cell tumors (NGCTs) or Stromal tumors (5%)</u>	
Leydig cell tumor	<ul style="list-style-type: none"> ❖ Like the Sertoli-Leydig cell tumor of the Ovary. ❖ Most often benign. characterized by intracytoplasmic Reinke crystals. ❖ ↑ Androgen and estrogen ❖ Associated with precocious puberty in children and with gynecomastia in adults
Sertoli cell tumor (Androblastoma)	<ul style="list-style-type: none"> • Also similar to the Sertoli-Leydig cell tumor of the ovary

Diseases of Prostate

Prostatitis	<ol style="list-style-type: none"> Acute bacterial prostatitis: Severe symptoms i.e fever e rigors, urgency, frequency On DRE: tender, boggy, and enlarged prostate Chronic bacterial prostatitis: Usually due to recurrent UTI with same strain, \pm symptoms Chronic prostatitis (chronic pelvic pain syndrome): Symptoms of chronic pelvic pain or symptoms on voiding in the absence of UTI Asymptomatic inflammatory prostatitis: Evidence of inflammation in the absence of genitourinary finding, usually an incidental finding
Benign prostatic hyperplasia (BPH)	<ul style="list-style-type: none"> ❖ Common in men > 50 years old ❖ Although BPH has no relation to prostate cancer, the two conditions can coexist. ❖ Characterized by smooth, elastic, firm nodular enlargement (hyperplasia does not hypertrophy) of periurethral (lateral and middle) lobes, which compress the urethra into a vertical slit. ❖ \uparrow free form PSA ❖ Clinical features: <ul style="list-style-type: none"> ○ Frequency, dysuria, hesitancy (difficulty in starting urination) ○ Urinary tract infection, hydronephrosis ○ Incomplete bladder emptying ❖ Treatment <ul style="list-style-type: none"> ○ α1-antagonists (terazosin, tamsulosin), which cause relaxation of smooth muscle. 5α-reductase inhibitors (e.g., Finasteride) ○ Surgical resection (e.g., TURP, ablation)
Prostatic carcinoma (CA)	<ul style="list-style-type: none"> ❖ Common in men > 50-60 years old. Mostly Adenocarcinoma type. ❖ Arises most often from posterior lobe (peripheral zone) of prostate. ❖ On DRE: Hard, irregular, firm nodule most likely suggests cancer ❖ \uparrow total PSA with fraction \downarrow of free PSA ❖ \uparrow prostatic acid phosphatase (PAP). ❖ \uparrow ALP (reflects metastasis to bone--Osteoblastic activity) ❖ Serum PSA levels are not sensitive indicator of CA prostate, while, they have role in monitoring recurrence and response to therapy ❖ Gleason's scoring is done for staging of prostate cancer. Low scoring e.g 6 indicates well differentiated tumor , while, high scoring e.g, 9 or 10 indicates high grade or undifferentiated tumor

FEMALE REPRODUCTION

Synthesis of estrogen & Progesterone	<ul style="list-style-type: none"> • Theca cells produce testosterone (stimulated at the first step by LH) • Androstenedione diffuses to the nearby Granulosa cells, which contain 17β-hydroxysteroid dehydrogenase, which converts androstenedione to testosterone, and aromatase, which converts testosterone to 17 β-estradiol (stimulated by FSH).
Regulation	<ol style="list-style-type: none"> 1. Hypothalamic control-GnRH Pulsatile release of GnRH stimulates the anterior pituitary to secrete FSH and LH. 2. Anterior lobe of the pituitary-FSH and LH FSH and LH stimulate the following in the ovaries: <ul style="list-style-type: none"> ❖ Steroidogenesis in the ovarian follicle and corpus luteum ❖ Follicular development beyond the antral stage ❖ Ovulation and Luteinization 3. Negative and positive feedback control by estrogen and progesterone

Hormone	Functions
Estrogen	<ul style="list-style-type: none"> ❖ Development of the breasts and secondary sex characteristics ❖ Maintains pregnancy. Stimulates Prolactin secretion but blocks its action on breast ❖ Both positive & Negative feedback effect on FSH & LH secretion ❖ Lowers uterine threshold to contractile stimuli during pregnancy ❖ Helps to maintain pregnancy ❖ Most common cause of breast atrophy is decreased estrogen ❖ Pre-menopausal breast atrophy is due to dec estrogen & dec progesterone ❖ Post menopausal breast atrophy is mainly due to low estrogen levels
Progesterone	<ul style="list-style-type: none"> ❖ Maintenance of endometrial thickness and pregnancy is the most important role ❖ Secretory phase of menstrual cycle. Breast lobules and alveoli development ❖ -Ve feedback effect on FSH and LH ❖ Raises uterine threshold to contractile stimuli during pregnancy
FSH & LH variations In male & females	<ul style="list-style-type: none"> ❖ In childhood hormone levels are lowest and FSH > LH

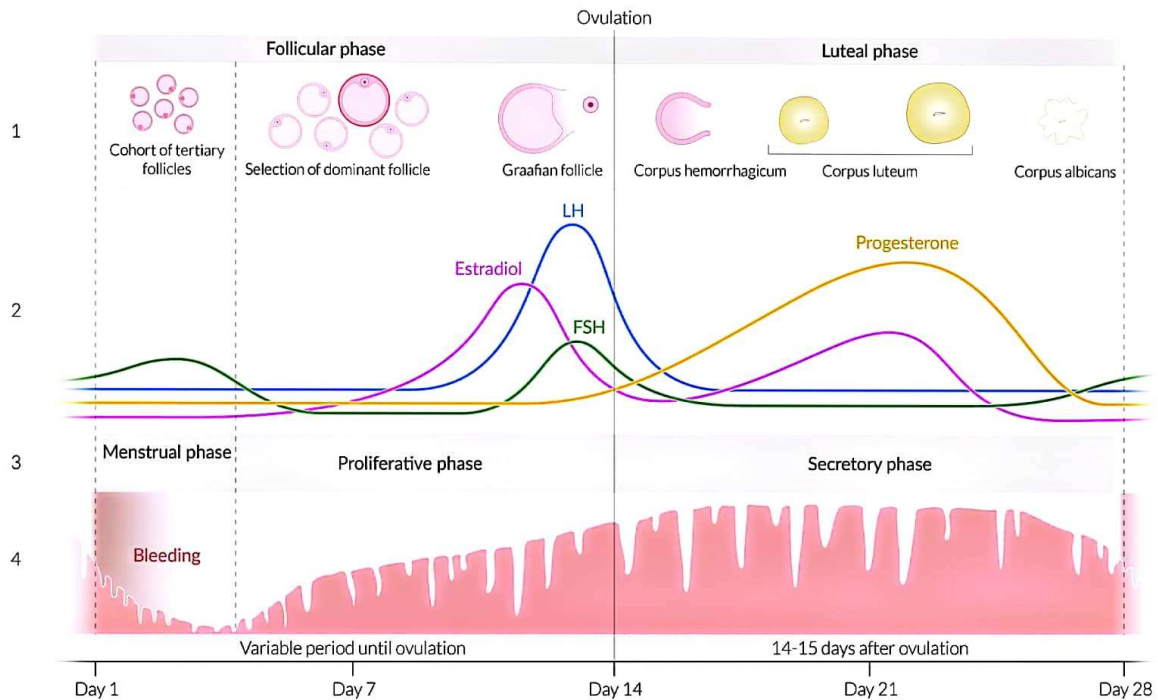
	<ul style="list-style-type: none"> ❖ At puberty and during the reproductive years, hormone levels increase and LH > FSH. In senescence, hormone levels are highest and FSH > LH
Estrogen variations in lifespan	<ul style="list-style-type: none"> ❖ Estrogen in Reproductive years (when a woman is like a doll → ESTRADIOL ❖ Estrogen in pregnancy ESTRADIOL- (tri-mom, dad, child (used for screening congenital abnormality). ❖ Estrogen in menopause: → ESTRONE... (ONE--woman becomes single again) ❖ Potency: estradiol > estrone > estriol

MENSTRUAL CYCLE

Follicular Phase (Days 0 To 14)	<ul style="list-style-type: none"> ❖ Hormone responsible: FSH mainly and LH partly. ❖ A primordial follicle → primary follicle (under the influence of FSH & LH) → mature Graafian follicle. Primordial follicle is lined by only single layer of cells ❖ LH and FSH receptors are up-regulated in theca and granulosa cells → ↑ Estrogen (Estradiol) ❖ ↑ Estradiol levels causes proliferation of the uterus. ❖ FSH and LH levels are suppressed by negative feedback effect of estradiol on the anterior pituitary. ❖ Progesterone levels are low.
Ovulation (day 14)	<ul style="list-style-type: none"> ❖ Hormone responsible: ↑ LH ❖ Occurs 14 days before menses, regardless of cycle length. Thus, in a 28-day cycle, ovulation occurs on day 14; in a 35-day cycle, ovulation occurs on day 21. ❖ A burst of estradiol synthesis at the end of the follicular phase has a positive feedback effect on the secretion of FSH and LH (LH surge). ❖ Ovulation occurs because of the estrogen-induced LH surge. ❖ Estrogen levels decrease just after ovulation (but rise again during the luteal phase). ❖ Cervical mucus increases in quantity; it becomes less viscous and more penetrable by sperm.
Luteal Phase (Days 14 To 28)	<ul style="list-style-type: none"> ❖ The corpus luteum begins to develop, and it synthesizes estrogen and progesterone. ❖ Vascularity and secretory activity of the endometrium increase to prepare for receipt of a fertilized egg. ❖ Basal body temperature increases because of the effect of progesterone on the hypothalamic thermoregulatory center. ❖ Fate Of Corpus Luteum: <ul style="list-style-type: none"> ○ If fertilization occur → ↑ corpus luteum size under the influence of hCG → secretes progesterone ○ If fertilization does not occur, the corpus luteum regresses → called corpus Albicans → As a result, estradiol and progesterone levels decrease abruptly.
Menses (Days 0 to 4)	<ul style="list-style-type: none"> ❖ The endometrium is sloughed because of the abrupt withdrawal of estradiol and progesterone.

Key Facts

- ❖ Main hormone for follicular phase (follicles development) is FSH. For Ovulation → LH surge
- ❖ Main hormone for proliferative phase is estrogen. For secretory phase is progesterone
- ❖ Hot flushes are due to estrogen deficiency
- ❖ In PCOS, LH:FSH ratio is 3:1. Two days before ovulation LH raises **6-10 folds**
- ❖ Secondary oocyte is formed under the influence of LH surge (not under FSH)
- ❖ Menopause is diagnosed by serum FSH levels. FSH & LH levels raised but estrogen decreased
- ❖ Placenta secretes estrogen, progesterone and Inhibin
- ❖ In case of Azoospermia, serum FSH and LH levels need to be investigated
- ❖ Lactational amenorrhea is due to inc prolactin > dec GnRH levels



PREGNANCY

Fertilization	<ul style="list-style-type: none"> ❖ If fertilization occurs, the corpus luteum is rescued from regression by human chorionic gonadotropin (HCG), which is produced by the placenta. ❖ Fertilization most commonly occurs in the upper end of fallopian tube (the ampulla). ❖ Occurs within 1 day of ovulation. ❖ Implantation within the wall of the uterus occurs 6 days after fertilization. ❖ Syncytiotrophoblasts (placenta) secrete hCG, which is detectable in blood 1 week after conception and in urine 2 weeks after conception.
1st Trimester	<ul style="list-style-type: none"> ❖ The corpus luteum (stimulated by HCG) is responsible for the production of estradiol and progesterone. Peak levels of HCG occur at gestational week 9 and then decline
2nd & 3rd Trimesters	<ul style="list-style-type: none"> ❖ Progesterone is produced by the placenta. ❖ Estrogens are produced by the interplay of the fetal adrenal gland and the placenta. ❖ The major placental estrogen is estriol. ❖ Human placental lactogen is produced throughout pregnancy. Its actions are like those of growth hormone and prolactin ❖ Testosterone synthesis in fetal life is under influence of human placental lactogen ❖ Growth hormones levels remain unchanged i.e same during pregnancy ❖ Gestational age (GA) is calculated from LMP ❖ Embryonic age is calculated from date of conception (GA-2 weeks)

PHYSIOLOGICAL CHANGES DURING PREGNANCY

CVS	<ul style="list-style-type: none"> ▪ ↑ Cardiac output (due to ↑ plasma volume, and hence ↑ venous return) → Heart enlarges slightly ▪ ↑ Cardiac output (↑ preload, ↓ afterload, ↑ HR → ↑ placental and uterus perfusion)
Blood	<ul style="list-style-type: none"> ▪ Plasma Volume Expansion: Blood volume ↑ by 30% (progesterone causes salt and water retention in kidneys, leading to plasma volume expansion, and “anemia of pregnancy”) ▪ Most common cause of low Hb in pregnancy is Hemodilution i.e physiological anemia of pregnancy ▪ Hb Amount And Concentration: ↑ RBC count → ↑ HB amount (but ↓ HB conc. due to plasma volume expansion) ▪ ESR: ↑ ESR (due to ↑ fibrinogen)
Respiratory	<ul style="list-style-type: none"> ▪ RR & Minute Ventilation: ↑ resp. rate (due to ↑ progesterone) → ↑ Minute ventilation ▪ Respiratory Volumes: Elevation of diaphragm → ↓ ERV + ↓ RV ↓ FRC, ↑ Tidal volume (by 40%) ▪ Resp Capacities: ↑ Inspiratory capacity (IRV), ↓ Expiratory capacity (ERV), ↓ Total lung capacity ↑ Vital capacity (by 100ml to 200 ml) ▪ Hyperventilation → dec pCO₂
Renal	<ul style="list-style-type: none"> ▪ GFR ↑ by 25% → ↑ Urine formation (+ ↓ Serum creatinine + ↓ Plasma urea level) ▪ ↑ Na⁺, Cl⁻, and H₂O reabsorption (due to ↑ progesterone, and ↑ aldosterone)
Endocrine	<ul style="list-style-type: none"> ▪ Anterior Pituitary Hormones: ↑ Secretion of (i) ACTH (ii) TSH (iii) Prolactin ↓ Secretion of (i) FSH and (ii) LH due to –ve feedback inhibition by estrogen and progesterone ▪ Adrenocortical Hormones: ↑ Cortisol secretion → Mobilizes amino acids from muscles of mother ↑ Aldosterone secretion → ↑ Reabsorption of Na⁺, Cl⁻, and H₂O ▪ Thyroid Hormones: ↑ T₃ + ↑ T₄ (due to ↑ thyroid binding globulins “TBG”) ▪ Parathyroid Hormone: ↑ PTH → ↑ Ca⁺ absorption from GIT, kidneys, and bones of mother
Metabolic	<ul style="list-style-type: none"> ▪ Carbohydrates: ↑ Blood glucose ▪ Proteins: ↓ Total proteins, ↓ Albumin, ↑ Globulin ▪ Lipids: ↑ Total lipids, ↑ Triglycerides, ↑ Cholesterol ▪ Mineral Metabolism: ↑ Ca⁺ absorption from GIT, kidneys, and bones, ↑ Fe⁺ need, ↑ Blood level of Na⁺ and Cl⁻ ▪ Vitamin Metabolism: ↑ Vit. D need, Vit. K should be given before birth to avoid hemorrhagic disease of the newborn
BMR	<ul style="list-style-type: none"> ▪ ↑ BMR (by 10 – 15%) → Pregnant woman feel overheated (hot flushes)

Ectopic pregnancy

- ❖ Defined as implantation of conceptus outside the uterine cavity
- ❖ Commonest site is the ampulla of fallopian tube in over 95% of cases
- ❖ Least common site is cervix
- ❖ Risk factors: Previous ectopic pregnancy, History of infertility, Previous PID or tubal surgery
- ❖ Clinical features: presents early in 6-7 weeks of 1st trimester with;
 - Classic triad of amenorrhea, vaginal bleeding, and abdominal pain (Hypochondrial pain)
 - Clinically mistaken for appendicitis. Ruptured cases present with shock like state
- ❖ Diagnosed via USG or Laparotomy. Laparotomy with salpingectomy is the preferred choice

Abnormalities of Placental Attachment

1. Placental abruption (abruptio placentae)

- Premature separation (partial or complete) of the placenta.
- This is an important cause of antepartum bleeding and fetal death.
- Risk factors: trauma (e.g.. motor vehicle accident), smoking, hypertension. preeclampsia
- It is often associated with disseminated intravascular coagulation (DIC)

2. Placenta accreta

- Defective decidua layer → abnormal attachment and separation after delivery
- Risk factors: prior C-section. Inflammation, placenta previa
- It is manifested clinically by impaired placental separation after delivery, sometimes with massive hemorrhage.

3. Placenta previa

- Attachment of placenta to lower uterine segment over (or <2 cm from) internal cervical os.
- Risk factors: multiparity, prior C-section.
- Associated with painless third trimester bleeding.

Gestational Trophoblastic Disease

GTDs Include disorders characterized by degenerative or neoplastic changes of trophoblastic tissue

Hydatiform Mole

- ❖ Characterized by cystic swelling of chorionic villi, accompanied by variable trophoblastic proliferation. Snowstorm appearance of complete mole on USG.
- ❖ Presentation: enlarged uterus, vaginal bleeding. ↑hCG
- ❖ Treatment: dilatation and curettage, methotrexate
- ❖ Two types

	Complete Mole	Partial Mole
Karyotype	46 XXX 46.XY	69 XXX 69. XXXY 69 XYY
Fetal Parts	No	Yes
Imaging	"Honeycombed uterus or "clusters of grapes", "snowstorm appearance on ultrasound	Fetal parts
Risk Of Choriocarcinoma	2%	Rare

Gestational Choriocarcinoma

- ❖ Aggressive malignant neoplasm that occurs more frequently than ovarian choriocarcinoma.
- ❖ An increased serum concentration of hCG is an important diagnostic sign.
- ❖ Characteristics include early hematogenous spread to the lungs.
- ❖ No chorionic villi present.
- ❖ Presents with abnormal ↑β-hCG shortness of breath, hemoptysis. Hematogenous spread to lungs → cannonball appearance.

Ovarian Tumors

Classification:

1. Surface epithelial tumors – most common,
2. Germ cell tumors
3. Sex cord stromal tumors
4. Metastatic

■ Surface Epithelial stromal tumors

Serous tumor	<ul style="list-style-type: none"> ❖ Most common ovarian neoplasm. ❖ Lined with fallopian tube-like epithelium. ❖ Often bilateral. Psammoma bodies present ❖ It may be benign, borderline or malignant
Mucinous tumor	<ul style="list-style-type: none"> • Multiloculated, large. Lined by mucus-secreting epithelium. • No Psammoma bodies • May extend to peritoneum forming pseudomyxoma peritonei
Endometrioid	<ul style="list-style-type: none"> ❖ Endometriosis (ectopic endometrium-like tissue) within ovary with cyst formation ❖ Chocolate cyst- endometrioma filled with dark, reddish- brown blood
Clear cell carcinoma	<ul style="list-style-type: none"> • Most commonly seen in association with endometriosis.
Brenner tumor	<ul style="list-style-type: none"> • They are characterized by small islands of epithelial cells resembling Bladder transitional epithelium interspersed within a fibrous stroma.

■ Germ cell tumors

Dysgerminoma	<ul style="list-style-type: none"> • Analogous to seminoma of testes
Yolk sac tumor or endodermal sinus tumor	<ul style="list-style-type: none"> ❖ This tumor is analogous to endodermal sinus tumor of the testis. ❖ It produces AFP
Teratoma	<ul style="list-style-type: none"> • Tumors derived from two or three embryonic layer • Types: simple teratoma or specialized type • Contains hair, skin, cartilage, teeth, thyroid or nervous tissue etc.

■ Sex cord stromal tumors

Fibroma	<ul style="list-style-type: none"> • Associated with Meig's syndrome: • a triad of ovarian fibroma, ascites, and hydrothorax
Granulosa cell tumor	<ul style="list-style-type: none"> ❖ Estrogen-secreting tumor causes precocious puberty. ❖ In adults, it is associated with endometrial hyperplasia or endometrial carcinoma. Call-Exner bodies →important diagnostic feature
Sertoli Leydig cell tumor	<ul style="list-style-type: none"> • Androgen-secreting tumor is associated with Virilism (masculinization)

■ Metastatic tumors

- **Krukenberg tumor:**
GI malignancy (most often stomach) that metastasizes to ovaries, **mucin-secreting signet cell** adenocarcinoma

NOTE: ovarian tumors metastasize via **Peritoneum > lymph nodes**

Polycystic Ovarian syndrome

- **Risk factors:** Genetic/family history, autoimmune diseases, Obesity, high androgens, metabolic syndrome, type 2 DM, HTN
- **PCOS Triad:** oligomenorrhea, hirsutism, polycystic ovaries on USG
- **Hormonal levels:** Increased levels of androgens (FSH, LH, Testosterone) and low cortisol levels
- **Treatment:** **1st line:** Weight loss and lifestyle modifications.
OCPs (nor-ethisterone), **cyproterone acetate for hirsutism**, flutamide, electrolysis/laser therapy

Diseases of the Uterus

Summary:

- Endometrial hyperplasia: Endometrial thickness of > 4mm. it may be simple or complex
- Fibroids (leiomyomas) are benign tumors of uterus. It causes heavy menstrual bleed (HMB)
Red degeneration of fibroid may occur in pregnancy that presents with acute abdomen
- Leiomyosarcoma is a rare malignant tumor, diagnosed by high mitotic rate and atypia
- Chronic Endometritis is diagnosed by Plasma cells on biopsy
- **Endometriosis:** presence of endometrial glands and stroma outside the uterus.
Multifactorial causes, early menarche and delayed child birth are risk factors. Age group 25-45 years, presents with chronic pelvic pain, dysmenorrhea, dyspareunia. Diagnosed by laparoscopy and biopsy. Give NSAIDs and hormonal therapies as no definite cure available
- **Adenomyosis:** presence of endometrial tissue inside the myometrium (not outside the uterus)
Age: ≥ 35 years, risk factors are multiparity and uterine surgery, presents with boggy, bloated or enlarged uterus with chronic pelvic pain, dyspareunia.
Hysterectomy is used for diagnosis and treatment
- Endometrial cancers spread by penetration into myometrium (direct spread) preferably, or via blood or lymphatics (least followed route)

	Type 1 Endometrial cancer	Type 2 Endometrial cancer
Age	50-60s, Pre/Peri-menopausal females	70s, Post-menopausal females
Risk factors	Chronic estrogenic stimulation, obesity, DM, nulliparity, anovulation, HNPCC	Endometrial atrophy Estrogen independent
Precursor lesions	Atypical endometrial hyperplasia	Less defined
Types	Endometrial adenocarcinoma mostly	Clear cell, papillary serous carcinoma
Genetics	PTEN mutation, MSH-1, MLH-2	P53
Metastasis	Lymph node, ovarian involvement	Peritoneum
Prognosis	Favorable due to low grade	Poor, aggressive course

Cervical cancer

- Squamous cell cancer of cervix is the 3rd most common gynecological malignancy
- Risk factors: HPV, multiparity, IUD, multiple sex partners, partner with multiple sex partners, tobacco smoking and nicotine.
HPV serotypes 6,11 cause benign lesions i.e warts, while, HPV 16,18,31 → malignancy
Cervical cancer presents with post coital bleeding, unusual vaginal discharge, vaginal bleeding between periods, menstrual bleeding that is longer or heavier than usual, pain during intercourse and pelvic pain.
- Pap smear or cervical cytology is used for diagnosis
- **Remember;**
 - ✓ Cause of cervical dysplasia → HPV > IUD
 - ✓ Cause of cervical metaplasia → Multiparity > IUD

BREAST**Lactation**

- ❖ Estrogens and progesterone stimulate the growth and development of the breasts throughout pregnancy. Prolactin levels increase steadily during pregnancy because estrogen stimulates prolactin secretion from the anterior pituitary,
- ❖ Lactation does not occur during pregnancy because estrogen and progesterone block the action of prolactin on the breast.
- ❖ After labor, estrogen and progesterone levels decrease abruptly, and lactation occurs.
- ❖ Lactation is maintained by suckling, which stimulates both oxytocin and prolactin secretion.
 - Prolactin-induces and maintains lactation and reproductive function.
 - Oxytocin-assists in milk letdown; also promotes uterine contractions.
- ❖ Ovulation is suppressed as long as lactation continues because prolactin has the following effects:
 - Inhibits hypothalamic GnRH secretion.
 - Inhibits the action of GnRH on the anterior pituitary and consequently inhibits LH and FSH secretion.
 - Antagonizes the actions of LH and FSH on the ovaries.

Breast Milk

- Breast milk is the ideal nutrition for infants < 6 months old.
- Breast milk is preferably to be given 30 minutes after birth of newborn
- Contains maternal immunoglobulins (passive immunity: mostly IgA), macrophages, lymphocytes
- Breast milk reduces infant infections and is associated with ↓ risk for child to develop asthma, allergies, diabetes mellitus, and obesity.
- Exclusively breastfed infants require vitamin D supplementation.
- Breastfeeding ↓ maternal risk of breast and ovarian cancer and facilitates mother-child bonding.
- **Breast milk is notoriously deficient in Iron, Vitamin C and D.** (vit C > vit D)
- Human milk has more content of lactose and water
- Cow milk has more salts (Na, K, Mg, Ca), more lactalbumin and casein than human milk

Fibrocystic disease (or) Lumpy bumpy disease	<ul style="list-style-type: none"> ❖ Most common disorder of the breast. ❖ It is uncommon before adolescence or after menopause. ❖ Usually, bilateral. ❖ Disease is postulated to result from increased activity of estrogen or decrease progesterone activity. ❖ Subtypes: <ul style="list-style-type: none"> ○ No proliferative forms (stromal fibrosis and cyst formation) are not associated with an increased risk of breast cancer. ○ Epithelial hyperplasia or sclerosing adenosis carries a slightly increased risk while the increased risk of cancer.
Fibroadenoma	<ul style="list-style-type: none"> ❖ Most common breast tumor in women younger than 25 years of age. ❖ Tumor is entirely benign, painless and is not a precursor of breast cancer.
Phylloides tumor	<ul style="list-style-type: none"> ❖ Large mass of connective tissue and cysts with "leaf-like" lobulations ❖ It is benign but there is rare risk of malignancy
Gynecomastia	<ul style="list-style-type: none"> ❖ Breast enlargement in males due to ↑ estrogen compared with androgen activity ❖ Causes: <ul style="list-style-type: none"> ○ Cirrhosis ○ Hypogonadism (e.g., Klinefelter syndrome) ○ Testicular tumors ○ Drugs → Spironolactone, Hormones, Cimetidine, Ketoconazole.

BREAST CANCER	<ul style="list-style-type: none"> ❖ Most common malignancy in females ❖ Risk factors→↑ estrogen exposure, older age at 1st live birth, obesity. Smoking, alcohol, obesity, Positive family history ❖ BRCA1 or BRCA2 gene mutations. Early menarche and late menopause ❖ Occurs most frequently in the upper outer quadrant (50%) of the breast ❖ Presents with lump/swelling, retracted nipple, bloody nipple discharge, palpable axillary lymph nodes in most cases ❖ Types: <ul style="list-style-type: none"> Non-invasive: <ul style="list-style-type: none"> ▪ Ductal carcinoma in situ ▪ Paget disease of the breast (eczema like presentation) ▪ lobular carcinoma of the breast Invasive: <ul style="list-style-type: none"> ▪ Invasive ductal carcinoma (most common type) ▪ Invasive lobular carcinoma – often bilateral, need prophylactic mastectomy ▪ Medullary carcinoma ▪ Mucinous carcinoma ▪ Inflammatory type (associated with peau d'orange appearance + lymphedema) ❖ Screening done via mammography (> 40 years) or USG (< 40 years of age) ❖ Mammography reduces the cancer risk by 33-40% ❖ Biopsy is done for diagnosis and histological typing ❖ Breast cancer most commonly metastasizes to axillary lymph nodes ❖ Sentinel lymph node is the first node draining the malignancy ❖ Axillary lymph node metastasis is the most important prognostic factor ❖ Staging is given in the diagram below. ❖ Nottingham histological grading is done on 3 criteria to assess prognosis: <ul style="list-style-type: none"> A. Tubule formation B. nuclear pleomorphism C. Mitotic count It takes account into histological grade, size and lymph node metastasis ❖ Treatment: <ul style="list-style-type: none"> ❖ Partial or radical mastectomy ❖ Chemotherapy ❖ Hormonal therapy: <ul style="list-style-type: none"> Tamoxifen (anti-estrogen drug) given in pre-menopausal women Anastrozole (aromatase inhibitors) given in post- menopausal women
----------------------	--

Breast Cancer Staging Diagram

TNM Classification ...

Tumour

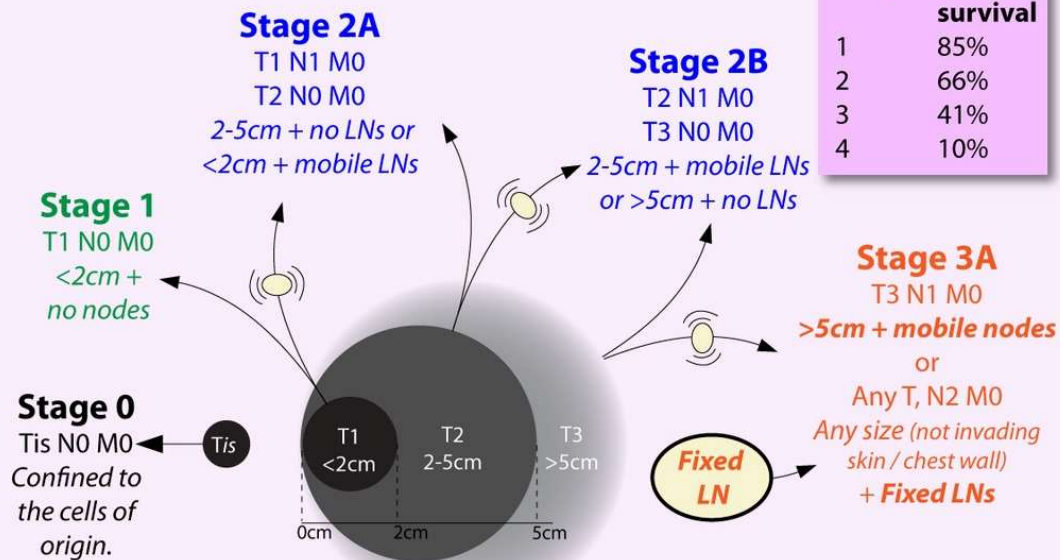
Tis - *in situ* carcinoma
 T1 - <2 cm diameter
 T2 - 2-5 cm diameter
 T3 - >5 cm diameter
 T4 - Invasion of skin / chest wall

Lymph Nodes (LNs)

N1 - ipsilateral LNs (mobile) (())
 N2 - ipsilateral LNs (fixed) ()
 N3 - **internal** mammary LNs

Metastases

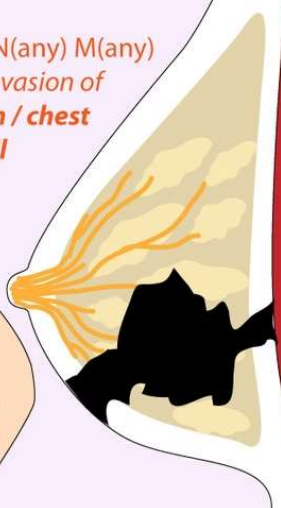
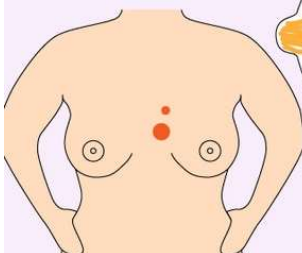
M0 - no distant mets
 M1 - distant mets
 or **supraclavicular** LNs



Stage 3B : either of ...

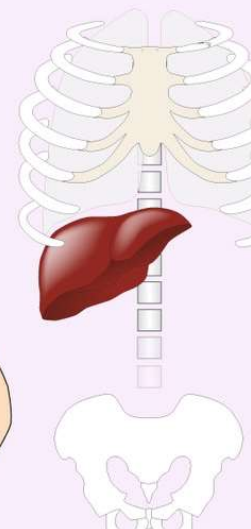
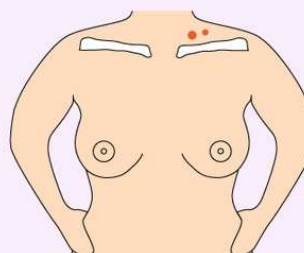
T(any) N3
 = **Internal mammary LNs** involved

T4 N(any) M(any)
 = Invasion of **skin / chest wall**



Stage 4

T(any) N(any) M1
Distant mets or Supraclavicular LNs.
 Typically to the lungs, liver and bones.



PAST PAPER BCQS + HIGH YIELD POINTS

1. At ovulation = Ferning test -Ve
2. Male external genitalia are formed by DHT. Internal genitalia by testosterone
3. Growth hormones levels remain unchanged in pregnancy
4. Less than 5% contraception failure chances for = vasectomy, tubal ligation, OCPs, IUCDs
5. Which layer is shed in menstruation = Functional layer of endometrium
6. Pregnant lady with dead fetus, labor induced but not responding due to = decrease oxytocin receptors on myometrium.
7. During pregnancy, lumen of uterine cavity is obliterated by fusion of = decidua capsularis and decidua parietalis
8. Peak levels of estradiol are seen at = Ovulation
9. LH increases 2 days before ovulation = 6-10 fold rise
10. Fetal blood leaving placenta having oxygen is = 30 mmHg (Umbilical vein, 80 % saturation)
11. Breast milk has more than cow milk = lactose and water
12. Action of oxytocin is potentiated in pregnancy by = estrogens
13. Estrogen is not produced by theca cells
14. Low levels of cholesterol in premenopausal women and protection from thromboembolism is done by = Estrogen
15. Fetal heart rate = 120-160 beats/minute
16. Progesterone is a precursor of aldosterone, cortisol and androstenedione
17. Lactation during pregnancy is inhibited by = estrogen & progesterone > estrogen
18. A lady having menstrual cycle of 32 days will ovulate at ? 32-14 → 18 th day
19. A female with cycle of 21-23 days, ovulation will occur at = 7-9 th day
20. In a female with 24 days menstrual cycle. When will ovulation occur = 10 th day from beginning (1 st day) of her last menstrual period (LMP)
21. Sperms are stored in epididymis
22. Best test to confirm pregnancy before 10 days is serum β- hCG.
23. Endometrium contains glands and tortuous arteries at = late secretory phase
24. After 10 days to confirm pregnancy → do urine pregnancy test
25. Preterm pregnancy is before 37 weeks. Term = 37-42 weeks. Post term → after 42 weeks
26. Corpus luteum maintained by = beta hCG
27. Investigation to be done in recurrent abortion = progesterone
28. At mid luteal phase, injection given to an athlete to delay menstruation = Progesterone > hCG
29. Softens the cervix = prostaglandins (PGs)
30. Fetal organ important for initiation of labor = fetal adrenal (cortisol) > fetal pituitary (ACTH).
31. Main steroid produced by fetal adrenal = dehydroepiandrosterone (DHEA)
32. Estrogen, progesterone actions occur through = intracytoplasmic receptors, as they are lipophilic hormones and cause activation of transcription factors (or via mRNA)
33. Sertoli cells release Inhibin and androgen binding protein.
34. Leydig cells release androgens i.e testosterone, under influence of LH
35. Testosterone is converted into 17-β estradiol under influence of = FSH
36. FSH is inhibited by inhibin. Lowest testosterone is seen in preschool age
37. Lab studies reveal Azoospermia, what further testing to be done for confirmation of infertility = FSH, LH levels. Remember, the gold standard for male subfertility is semen analysis. But in this case, the semen analysis has already done before which yields azoospermia, hence, only do FSH, LH to confirm diagnosis
38. After ovulation, ovum is at which stage = Metaphase of meiosis II
39. Oocyte at ovulation is = secondary oocyte
40. A lady having hyperemesis gravidarum is at risk of = Metabolic alkalosis
41. Important for 2 nd stage of labor = abdominal contractions
42. Corpus luteum maintain pregnancy for = 1-8 weeks. It secretes estrogen, progesterone and inhibin
43. Sperms stay active upto 48 hours. Life span of sperm is upto 72 hours
44. Max life of sperm in female genital tract = 24-72 hours
45. Full sperm regeneration occurs in = 64 days
46. A healthy newborn is given feed after = half an hour
47. 15-20 lactiferous ducts present in mammary glands

48. Seminal fluid has maximum concentration of = fructose
49. Cause of endometrial hyperplasia = estrogen exposure
50. Mid luteal phase hormone = Progesterone
51. Uterine artery pulsatility detected through Doppler at the earliest = 7 th week
52. A change that helps in lactation = Lobular hyperplasia
53. How much duration gap should be between children for family planning = 2-3 years
54. Fertilin at sperm head helps in adherence of sperm head to ovum membrane
55. Vaginal adenosis is a type of metaplasia
56. Weight of hCG is 39000
57. Primigravida taking iron tablets, lots of fresh vegetables and juices, what deficiency she is at risk of = Calcium (iron decreases absorption of calcium)
58. During lactation, what happens = Primordial follicles fail to develop
59. 60 year old male experiences urinary frequency, urgency, hesitancy. DRE reveals enlarged, rubbery and nodular prostate. The pathogenesis is related to = DHT. The diagnosis is BPH
60. DHT is a major growth factor for prostatic tissue that plays role in BPH pathogenesis
61. Firm, hard, asymmetric prostate on examination = CA prostate. PSAP and ALP raised
62. Most potent anabolic hormone = testosterone
63. Most imp effect on testosterone production is of = LH
64. Removal of testes may lead to loss of libido and depression
65. Onset of puberty is due to = pulsatile release of GnRH
66. Sick cell anemia patient experiences painful erection, it is called priapism. Trazodone most commonly associated with priapism. intracavernous injection of phenylephrine/epinephrine can be given to relieve it
67. Sperms of 70 yr. old man are asthenospermic (lack the progressive motility)
68. Hypospadias: urethral meatus open on ventral side of penis.
69. Purulent discharge from penis after unprotected sex, gram staining -Ve → Chlamydia trachomatis
70. 2 year old boy having only one palpable testes and palpable mass in left inguinal region = Cryptorchidism or undescended testis. It may lead to cancer and infertility.
71. 30 year old man with painless enlargement of testes + raised serum hCG = Seminoma (extremely radiosensitive tumor)
72. Mother of a 3 year old boy notices abnormal mass in scrotum, on work up AFP levels are high. Most likely condition = Yolk sac tumor or endodermal sinus tumor
73. Painless palpable swelling in testes of 60 years old man, raised LDH levels = diffuse large B cell lymphoma of testes (most common tumor of testes in men over 60 years old DLBCL)
74. Cottage cheese like vaginal discharge with itching = Candida Albicans.
75. Fishy odor with clue cells on pap smear = Bacterial vaginosis – Gardenella vaginalis involved
76. 33 years old lady presented with complaints of dysmenorrhea. On Laparoscopic examination, red blue nodules covering ovaries and uterine ligaments were seen. The condition = endometriosis
77. Highly suggestive of HPV infection are = Koilocytes
78. Risk factors of type 1 endometrial cancer = DM, obesity, HTN, nulliparity, anovulation, HNPCC
79. Cauliflower shaped perineal lesions i.e condyloma acuminatum is due to = HPV (6, 11 serotypes)
80. On routine examination, it is discovered that a 32 year old man exposed in utero to Diethylstilbestrol administered to her mother. She is at risk of = vaginal clear cell adenocarcinoma
81. Lab studies of a 27 years old obese lady reveal raised LH and testosterone. A pelvic USG will reveal = multiple follicular cysts in ovary. (Diagnosis: PCOS)
82. 24 year old lady complaints of left sided abdominal pain. Imaging shows enlarged left ovary with multiple calcifications. Laparoscopy reveals adnexal torsion and ovarian tumor. It is most likely which tumor = Dermoid cyst or mature teratoma. Calcifications are highly suggestive of teratoma
83. Findings in granulosa cell tumor = Call-Exner bodies
84. Soon after delivery, mother develops dyspnea, shock, multiorgan failure. On autopsy, masses of debris, squamous cells found in pulmonary microcirculation. The cause of death = amniotic fluid embolism
85. 1cm mass in upper outer quadrant of breast in a 65 years old lady = Breast cancer
86. Solitary discrete, firm, rubbery, freely mobile lesion, well circumscribed, non tender, in the breast of a 20 year old girl = Fibroadenoma (also called breast mouse)
87. Bloody nipple discharge may be seen in breast cancer or papilloma of breast

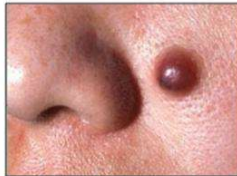
88. 57 years old lady presented with pain in left breast, On exam the left breast is red, swollen and warm to touch. The is significant dimpling (peau d' orange) of breast. Left Nipple is completely retracted. The diagnosis = Inflammatory carcinoma of breast
89. BRCA-1 mutation is a risk factor for = breast cancer
90. Estrogen in menopause = estrione
91. Respiratory changes in pregnancy = dec TLC, inc TV, unchanged VC and RR
92. In pregnancy P _{CO2} levels fall due to hyperventilation
93. Prostaglandins initiate cervical ripening by = hydration of collagen tissue
94. For Necrotic growth on cervix, the recommended radiation dose = 7000-8000 radons
95. Which contributes to formation of corona radiata = granulosa cells
96. Full development and function of seminiferous tubules require = FSH and androgens
97. Leydig cells have high levels of = Smooth endoplasmic reticulum
98. Factor involved in conversion of testosterone to estradiol = Aromatase enzyme, FSH hormone
99. Sperms after its formation in seminiferous tubules are stores at = ampulla of vas deferens
100. Uterine changes during pregnancy = hyperplasia + hypertrophy
101. Increase in oxytocin effect on cervix = cervix dilates
102. Partially motile sperms are present in = epididymis
103. PTU can cross placenta
104. Normal amniotic fluid at term = 800 ml
105. Maternal mortality ratio is the number of maternal deaths during a given period per live births during that period
106. Failure to lactate in pregnancy is due to = estrogen/progesterone
107. When sperms reach epididymis their movements become bidirectional
108. Main role of estrogens = secondary sexual characteristics
109. Main role of progesterone = maintenance of endometrial thickness > secretory phase
110. Maternal mortality rate is the number of maternal deaths in a given period per population of women who are of reproductive age group (15-45 years)
111. Lowest maternal mortality in age group = 20-30
112. Iron requirement In pregnancy = 800 mg, while, Ca requirement = 1200 mg
113. Acrosomal cap is formed by = Golgi complex
114. Mid cycle cervical mucus has = inc viscosity
115. Progesterone in OCPs work by = inhibition of ovulation, thickening of cervical mucus
116. Which remain dominant after puberty = primordial germ cells
117. Final or Last stage of puberty = Menarche. Remember (TAM = thelarche, adrenarche, menarche)

SKIN & MUSCULOSKELETAL SYSTEM

Bulla
Circumscribed
collection of
free fluid > 1 cm



Macule
Circular flat
discoloration
< 1cm
brown, blue, red or
hypopigmented



Nodule
Circular, Elevated,
Solid Lesion
> 1 cm



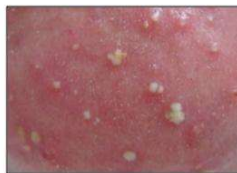
Patch
Circumscribed
Flat Discoloration
> 1cm



Papule
Superficial solid
elevated, ≤ 0.5 cm,
color varies



Plaque
Superficial elevated
solid flat
topped lesion
> 1 cm



Pustule
Vesicle containing
puss (inflammatory
cells)



Vesicle
Circular collection
of free fluid
 ≤ 1 cm



Wheal
Edematous,
transitory, plaque,
may last few hours



Scale
Epidermal thickening;
consists of flakes of
plates of compacted
desquamated layers
of stratum corneum



Crust
Dried serum or
Exudate on skin



Fissure
Crack or split



Excoriation
Linear erosion



Erosion
Loss of epidermis
superficial; part or all of
the epidermis has been
lost



Lichenification
Thickening of the
epidermis seen with
exaggeration of
Normal skin lines



Scar
Thickening; permanent
fibrotic changes that
occur on the skin
following damage of
the epidermis

DERMATOLOGICAL TERMS AND DISORDERS (SUMMARY)

Hyperkeratosis	Inc thickness of stratum corneum (e.g. psoriasis)
Parakeratosis	Retention of nuclei in stratum corneum (e.g. actinic keratosis, psoriasis)
Acanthosis	Epidermal hyperplasia of stratum Spinosum (e.g, Psoriasis , acanthosis nigricans)
Acantholysis	Separation of epidermal layers seen in Pemphigus vulgaris
Dyskeratosis	Abnormal premature keratinization (e.g, squamous cell carcinoma)
Albinism	Decreased tyrosinase activity, low melanin production despite normal melanocytes
Vitiligo	Autoimmune destruction of melanocytes - irregular patches of depigmentation
Melasma	Acquired hyperpigmentation associated with pregnancy or OCP use
Seborrheic dermatitis	Associated with Malassezia spp. Erythematous demarcated plaques with greasy yellow scales in areas rich in sebaceous glands such as scalp, face and peri-ocular
Atopic dermatitis (Eczema)	Type 1 HSR, pruritic eruption on skin flexures, association with atopic diseases e.g, asthma, skin/food allergies. Inc serum IgE levels. Often appears on face in infancy
Allergic contact dermatitis	Type IV HSR secondary to contact allergens (e.g, Nickel, poison ivy, neomycin) Remember, No antibodies involved in type IV HSR
Acne	Multifactorial causes, inc sebum/androgen production, abnormal keratinocyte desquamation, cutibacterium acnes colonization of pilosebaceous unit (comedones), and inflammation (papules/pustules, nodules, cysts)
Rosacea	Erythematous papules and pustules, but no comedones. May be associated with facial flushing in response to external stimuli (e.g, alcohol, heat)
Psoriasis	Papules and plaques with silvery scaling , especially on knees and elbows Auspitz sign – pin point bleeding spots when scales are scraped off
Urticaria	Type 1 HSR, pruritic wheals that form after mast cell degranulation. Superficial dermal edema with lymphatic dilation
Angiosarcoma	Hepatic angiosarcoma associated with vinyl chloride and Arsenic (in farmers) Associated with radiation therapy, typically on head, neck and breast regions
Bacillary angiomatosis	Benign capillary skin papules found in AIDS, caused by bartonella infections Frequently mistaken for Kaposi sarcoma, but has neutrophilic infiltration
Glomus tumor	Benign, painful, red-blue tumor, commonly under fingernails. Arises from modified smooth muscles of thermoregulatory glomus body.
Impetigo	Highly contagious, honey-colored crusting involving superficial dermis, usually from S aureus or S pyogenes infections
Erysipelas	Infection from S pyogenes involving upper dermis and subcutaneous tissue. Well defined raised demarcation between infected and normal skin
Abscess	Collection of pus from a walled off infection within deeper skin layers Almost always, the cause is S aureus .
Staphylococcal scalded skin syndrome	Exotoxin destroys keratinocyte attachments in stratum granulosum only Features: fever, generalized erythematous rash with sloughing of upper epidermis Commonly seen in newborns and children/adults with CKD. Nikolsky sign +Ve → separation of epidermis upon manual skin stroking
Necrotizing fasciitis	Surgical emergency, deeper tissue injury, usually from anaerobic bacteria or S pyogenes , presents with severe pain + Crepitus . Violaceous color of bullae
Molluscum contagiosum	Umbilicated papules in children caused by Pox virus/ sexually transmitted in adults
Hairy leukoplakia	White painless plaques on lateral tongue that can't be scraped off EBV mediated, in patients with immunosuppression (e.g, HIV or organ transplants)
Pemphigus vulgaris	Type 2 HSR, seen in older adults, IgG antibodies against desmoglein-1 and/or desmoglein-3 (component of desmosomes). Potentially fatal. Nikolsky sign +Ve, flaccid intraepidermal bullae caused by acantholysis Row of tombstones on H & E stain, oral mucosa involved Immunofluorescence shows reticular pattern around epidermal cells.
Bullous pemphigoid	Type 2 HSR, seen in older adults, IgG antibodies against hemidesmosomes Nikolsky sign - Ve, tense blisters containing eosinophils, oral mucosa spared Immunofluorescence shows linear pattern at dermo-epidermal cells.

Dermatitis herpetiformis	Deposits of IgA at tips of dermal papillae, associated with celiac disease Pruritic papules, vesicles and bullae (on knees, elbows, buttocks)
Erythema multiforme	Target lesions present, or multiple types of lesions- macules, papules, vesicles Associated with infections (e.g, mycoplasma pneumoniae), drugs (sulfa drugs)
Erythema nodosum	Often idiopathic, but may be due to sarcoidosis, TB, leprosy, IBD or staphylococcal infections. Painful raised lesion of superficial fascia on anterior shins
Steven Johnson syndrome (SJS)	Usually associated with a severe drug reaction, presents with fever, bullae, necrosis, sloughing of skin at dermo-epidermal junction. Mucous membranes involved Nikolsky +Ve, high mortality rate. Toxic epidermal necrolysis is severe form of SJS involving > 30% body surface area
Venous ulcer	Most common ulcer type, involves Gaiter area (typically medial malleoli) Irregular borders, associated with varicose veins, edema, stasis dermatitis
Arterial ulcer	Due to peripheral arterial disease, involves pressure points - distal toes, anterior shin Symmetric with well defined punched out appearance Associated signs: cold, pale, atrophic skin with hair loss and nail dystrophy.
Neuropathic ulcer	Due to peripheral neuropathy (e.g., diabetic foot), involves bony prominences e.g metatarsals heads, heel. Hyperkeratotic edge with undermined margins . Pain absent
Acanthosis nigricans	Associated with insulin resistance (e.g, obesity, diabetes, PCOS, cushing syndrome) or visceral malignancy e.g Gastric/pancreatic adenocarcinoma Epidermal hyperplasia causing symmetric hyperpigmented skin thickening especially in axilla or neck
Actinic keratosis*	Premalignant lesion on sun exposed areas (e.g cheeks) that may require excision Inc risk of skin squamous cell Cancer
Lichen planus*	Associated with hepatitis C, mucosal involvement manifests as Wickham striae. Pruritic, purple , polygonal planar papules and plaques
Pityriasis rosea	Herald patch, followed days later by other scaly erythematous plaques in Christmas tree distribution on trunk. Multiple pink plaques with collarlike scale
Sunburn	Acute inflammatory reaction due to excessive UV-B radiations Causes DNA mutations or apoptosis of keratinocytes UV-A involved in tanning and photoaging. Exposure to UVA UVB inc risk of skin cancer
BURN	
Superficial burn	Painful, involves epidermis only, localized blanching redness, no blisters
Superficial partial thickness burn	Painful to air and temperature, involves epidermis + papillary dermis. Blisters, blanches with pressure, swollen, warm
Deep partial thickness burn	Painless, perception of pressure only, involves epidermis + reticular dermis Blisters (easily unroofed), does not blanch with pressure
Full thickness burn	Painless, perception of deep pressure only, involves epidermis + full thickness dermis White, waxy, dry leathery, does not blanch with pressure.
SKIN CANCER	
Basal cell carcinoma (BCC)	Most common skin cancer, locally invasive but rarely metastasizes. White, pearly nodule, commonly with telangiectasia, Rolled borders Appears as non healing ulcer that bleeds on touch and infiltrative growth or as a scaling plaque. Tumor has Palisading nuclei . Nodular BCC is the most common type BCC more common on Upper lip , sun exposed areas of body (e.g, face)
Squamous cell carcinoma (SCC)	2 nd common skin cancer, more common on lower lip , face, ear, hands Association with immunosuppression, chronic non healing wounds, Arsenic exposure Histology shows Keratin pearls Bowen disease > actinic keratosis is linked with SCC of skin
Keratoacanthoma	Dome shaped nodule with keratin filled center seen in middle aged and elders Rapidly growing and resembles SCC
Melanoma	Aggressive tumor, in fair skin tone individuals, S-100 marker Depth of tumor (Breslow thickness) correlates with risk of metastasis 4 main Types: superficial spreading (most common) , nodular, lentigo maligna, acral lentiginous

BONE

Osteoblasts	<ul style="list-style-type: none"> ❖ Build the bone by secreting collagen and catalyzing mineralization in alkaline environment via ALP. Differentiates from mesenchymal stem cells in periosteum. ❖ RANKL (RANK ligand) is present on osteoblasts. ❖ RANK-RANKL interaction is important in bone resorption
Osteocytes	<ul style="list-style-type: none"> ❖ Mature bone cells
Osteoclasts	<ul style="list-style-type: none"> ❖ Dissolves bone by secreting H⁺ and collagenases. ❖ Differentiates from a fusion of monocyte/macrophage lineage precursors i.e., they have different origin from other bone cells. ❖ RANK receptor is receptor from TNF family that is present on Osteoclasts

Metabolic Bone Diseases

Osteoporosis	<ul style="list-style-type: none"> ❖ Characterized by a decrease in bone mass. ❖ Normal bone mineralization and lab values (serum Ca₂ + and PO₄). ❖ Cause may be impaired synthesis or increased resorption of bone matrix protein because of <ul style="list-style-type: none"> ○ Postmenopausal state (estrogen deficiency is a presumptive cause) ○ Physical inactivity, Hypercorticism, Hyperthyroidism, Calcium deficiency ○ Can be secondary to drugs (e.g., steroids, alcohol, anticonvulsants anticoagulants, thyroid replacement therapy) ❖ It results in bone structures inadequate for weight bearing can lead to vertebral Compression fractures. ❖ Diagnosed by a DEXA scan
Osteomalacia	<ul style="list-style-type: none"> ❖ Vitamin D deficiency in adults. Defective calcification of osteoid matrix- main feature ❖ When secondary to renal disease, Osteomalacia is called renal osteodystrophy
Rickets	<ul style="list-style-type: none"> ❖ Vitamin D deficiency in children's. Defective calcification of osteoid matrix ❖ Clinical manifestations include: <ul style="list-style-type: none"> ○ Craniotabes (soft skull) → thinning and softening of occipital and parietal bones. ○ Rachitic. rosary thickening of the Costochondral junctions that results in a string of-beads-like appearance. ○ Pigeon chest caused by protrusion of the sternum. ○ Bowed legs (genu varum) ○ Widening and metaphyseal cupping/fraying in rickets
Paget disease of bone (Osteitis deformans)	<ul style="list-style-type: none"> ❖ Disorder of bone remodelling caused by ↑ osteoclastic activity followed by ↑ osteoblastic activity that forms poor-quality bone and mosaic pattern. Complications: <ul style="list-style-type: none"> ○ Bone pain resulting from fractures: although bone is thick, it lacks strength; fractures can lead to deformity. ○ High-output cardiac failure can result from multiple functional arteriovenous shunts within highly vascular early lesions. ○ Hearing loss is caused by narrowing of the auditory foramen or direct involvement of the bones of the middle ear. ○ Osteosarcoma occurs in approximately 1% of cases
Osteopetrosis (Marble bone disease)	<p>Failure of normal bone resorption due to defective osteoclasts →→ thickened, dense bones that are prone to fracture. Also known as Albers-Schonberg disease.</p> <ul style="list-style-type: none"> ❖ impair ability of osteoclast to generate acidic environment necessary for bone resorption. Defective osteoclasts cause overgrowth and sclerosis of cortical bone. ❖ it is associated with anemia because of decreased marrow space, and with blindness, deafness, and cranial nerve involvement because of narrowing and impingement of neural foramina. ❖ X-rays show diffuse symmetric skeletal sclerosis (bone-in-bone. "stone bone") ❖ Bone marrow transplant is curative

Achondroplasia

- ❖ Most common cause of dwarfism.
- ❖ Autosomal dominant disorder is caused by a mutation in the fibroblast growth factor receptor 3 (FGFR3) gene.
- ❖ Short limbs with a normal-sized head and trunk are characteristic (large head relative to limbs)
- ❖ Membranous ossification is affected.

Osteitis Fibrosa Cystica (Von Recklinghausen Disease Of Bone)

- ❖ The cause is primary or secondary hyperparathyroidism.
- ❖ Widespread Osteolytic lesions are characteristic. Cystic bone spaces filled with brown fibrous tissue ("brown tumor")
- ❖ Brown discoloration resulting from hemorrhage with deposited hemosiderin.

Lab Values in Bone Disorders

Disorder	Serum Ca ²⁺	PO ₄ ³⁻	ALP	PTH	Notes
Osteoporosis	↓ bone mass
Osteopetrosis	.../↓	Ca ²⁺ ↓ in severe form
Paget disease of bone	↑	...	Abnormal "mosaic" bone architecture
Osteitis fibrosa cystica Primary hyperparathyroidism	↑	↓	↑	↑	"Brown tumors" Idiopathic or parathyroid hyperplasia, adenoma, carcinoma
Secondary hyperparathyroidism	↓	↑	↑	↑	Often as Compensation for CKD (↓ PO ₄ ³⁻ excretion and production of activated vitamin D)
Osteomalacia/Rickets	↓	↓	↑	↑	Soft bones: vitamin D deficiency also causes 2° hyperparathyroidism
Hypervitaminosis D	↑	↑	...	↓	Caused by over supplementation or granulomatous disease (e.g, sarcoidosis)

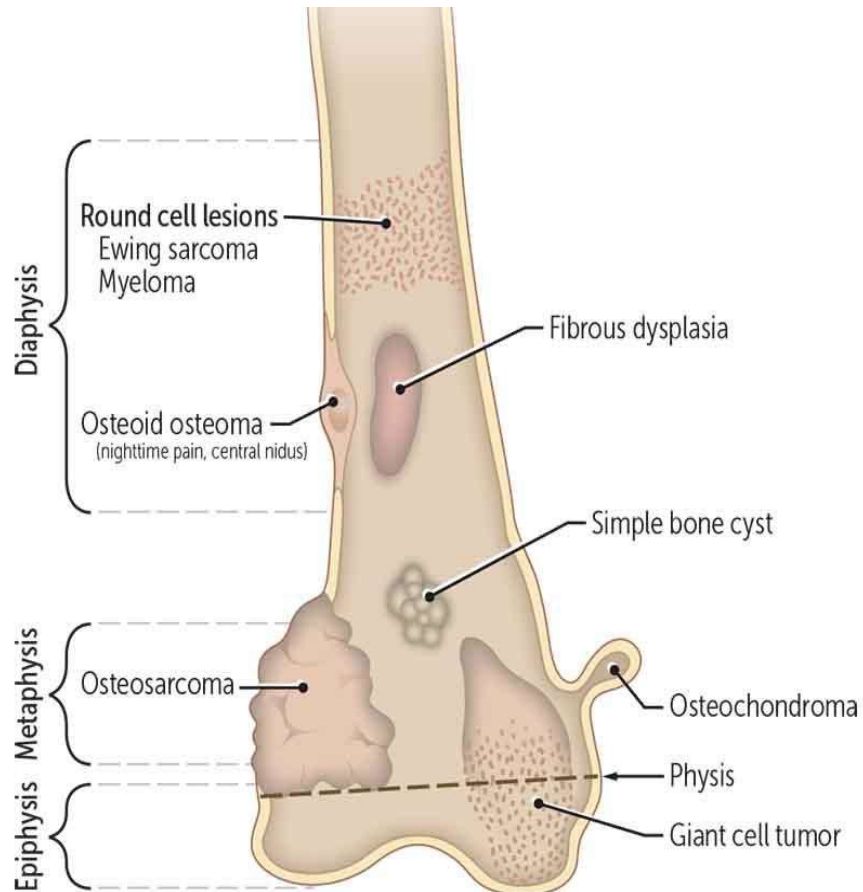
BONE TUMORS

Remember the **GEO-MED** Mnemonic for location.

- Giant cell-Epiphysis
- Osteosarcoma --- Metaphysis
- Ewing sarcoma --- Diaphysis

Type	Epidemiology/Location	Characteristic
<u>Benign Tumors</u>		
Osteochondroma	<ul style="list-style-type: none"> ❖ Most common benign tumor of bone ❖ Most frequently in men younger than 25 years of age. ❖ Most often originates from the metaphysis of long bones, with the lower end of the femur or the upper end of the tibia being favored locations 	Bone growth is covered by a cap of cartilage projecting from the surface of a bone (exostosis) Transformation to Chondrosarcoma is rare
Giant cell tumor (Osteoclastoma)	<ul style="list-style-type: none"> ❖ Peak incidence ⇒ 20-40 years Tumor occurs most often on the epiphyseal end of long bones; more than 50% occur around the knee. 	X-ray "Soap bubble" appearance
Osteoid Osteoma	<ul style="list-style-type: none"> ❖ Adults < 25 years old, Cortex of long bones ❖ Presents as bone pain worse at night that is relieved by NSAIDS (e.g, aspirin) 	Bone mass < 2 cm with radiolucent osteoid core
Osteoblastoma	<ul style="list-style-type: none"> ❖ Vertebrae of males > females ❖ Pain is NOT relieved by NSAIDs (e.g, Aspirin) 	Larger size > 2cm, similar histology to osteoid osteoma

Malignant Tumors		
Osteosarcoma	<ul style="list-style-type: none"> ❖ Most common primary malignant tumor of bone ❖ Tumor occurs most frequently in the metaphysis of long bones; the proximal portion of the tibia and most distal portion of the femur (around the knee) are preferred sites. ❖ Presents as painful enlarging mass or pathological fractures. 	X-ray: Codman triangle (from elevation of periosteum) Or sunburst pattern Predisposing factors Paget disease of bone, chondroma, ionizing radiation Familial retinoblastoma
Ewing sarcoma	<ul style="list-style-type: none"> ❖ Peak incidence → Boys < 15 years old. ❖ Commonly appears in diaphysis of long bones, especially femur, pelvic, flat bones e.g, scapula, ribs. ❖ Aggressive with early metastasis but responsive to chemotherapy ❖ Onion skin periosteal reaction in bone 	"Small blue cell" malignant tumor 11:22 chromosomal translocation. Mnemonic: 11 + 22 = 33 (Patrick Ewing's jersey number).
Chondrosarcoma	<ul style="list-style-type: none"> ❖ Medulla of pelvis, femur, and humerus 	Malignant chondrocytes



DISEASES OF JOINTS

	Osteoarthritis	Rheumatoid arthritis
Pathogenesis	<ul style="list-style-type: none"> ❖ Non-inflammatory joint disease is characterized by degeneration of articular cartilage. ❖ Osteoarthritis is most often related to mechanical trauma to the affected joints ("wear and-tear" arthritis) 	<ul style="list-style-type: none"> ❖ Chronic inflammatory disorder primarily affects the synovial joints ❖ Autoimmune disorder and Associated with HLA-DR4 (4 walls in a rheum (room))
Presentation	<ul style="list-style-type: none"> ❖ Asymmetric joint involvement. ❖ Morning stiffness of <15 minutes ❖ Improving with rest. ❖ Pain in weight-bearing joints after use ❖ Knee cartilage loss begins medially ("bow legged"). 	<ul style="list-style-type: none"> ❖ Symmetric joint involvement ❖ Morning stiffness of > 1 hour ❖ Improving with activity ❖ Systemic symptoms (fever, fatigue, weight loss).
Joint Findings	<ul style="list-style-type: none"> ❖ Heberden's nodes→ prominent osteophytes at DIP joints ❖ Bouchard's nodes→ prominent osteophytes at PIP joints ❖ Involves DIP and PIP, but not MCP 	<ul style="list-style-type: none"> ❖ Swan-Neck deformity ❖ Boutonniere deformity ❖ Cervical joint involvement most commonly C1,C2 always perform X-ray cervical spine before ETT ❖ Involves MCP, PIP, wrist; not DIP ❖ Ulnar deviation of fingers
Radiographic Hallmarks	<u>Mnemonic: LOSS</u> <ul style="list-style-type: none"> ❖ Loss of joint space-- typically non-uniform ❖ Osteophytes ❖ Subarticular sclerosis ❖ Subchondral cysts 	<ul style="list-style-type: none"> ❖ Loss of joint space- typically uniform ❖ Soft tissue swelling ❖ Erosions ❖ Periarticular osteopenia
Lab Findings	<ul style="list-style-type: none"> ❖ RA factor→ negative ❖ ESR, CRP → normal ❖ Anti-CCP →negative 	<ul style="list-style-type: none"> ❖ RA factor positive (70%- non-specific, IgM antibody that targets IgG Fe region) ❖ ESR, CRP raised ❖ Anti-CCP positive (90%-more specific)
Extra articular manifestations		<ul style="list-style-type: none"> ❖ Felty's Syndromes→ RA Splenomegaly+ Neutropenia ❖ Caplan Syndrome→ RA+ Pneumoconiosis + Lung Nodules ❖ AA amyloidosis, Sjögren syndrome, scleritis, carpal tunnel syndrome.
Treatment	<ul style="list-style-type: none"> ❖ Acetaminophen, NSAIDs, intra-articular glucocorticoids. 	<ul style="list-style-type: none"> ❖ NSAIDs, glucocorticoids, ❖ DMARD's (methotrexate, sulfasalazine, hydroxychloroquine) ❖ Biologic agents (eg, TNF-a inhibitors)

Poor Prognostic Features	<ul style="list-style-type: none"> ○ Rheumatoid factor positive, Anti-CCP antibodies, HLA DR4, Poor functional status at presentation ○ X-ray: early erosions (e.g., after < 2 years) ○ Extra articular features e.g., nodules ○ Insidious onset & Female gender is associated with a poor prognosis.
Other Conditions Associated with Positive RF	<ul style="list-style-type: none"> ○ Sjogren's syndrome (around 100%), Felty's syndrome (around 100%) ○ Cryoglobulinemia II & III 40-100%, Infective endocarditis (= 50%), SLE (= 20-30%), Systemic sclerosis (= 30%)
Extra-Articular Complications with Rheumatoid Arthritis	<u>Respiratory:</u> <ul style="list-style-type: none"> ❖ Pulmonary fibrosis & nodules, pleural effusion, bronchiectasis (especially nonsmokers), bronchiolitis obliterans, complications of drug therapy e.g.,

	<p>methotrexate pneumonitis, infection (possibly atypical) secondary to immunosuppression</p> <p>Ocular:</p> <ul style="list-style-type: none"> ❖ keratoconjunctivitis sicca (most common), episcleritis (erythema), scleritis (erythema and pain), keratitis, corneal ulceration, steroid-induced cataracts, chloroquine retinopathy <ul style="list-style-type: none"> • Osteoporosis • Amyloidosis (AA) • Felty's syndrome ❖ RA + splenomegaly + low white cell count+ leg ulcer in chronic seropositive RA <ul style="list-style-type: none"> • Caplan's syndrome ❖ RA+ Pneumoconiosis + Lung Nodules
Management of RA	<p>Initial therapy: (NICE guidelines 2009)</p> <ul style="list-style-type: none"> ❖ Patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD), plus short-term glucocorticoids. <p>DMARDs:</p> <ul style="list-style-type: none"> ❖ Methotrexate is the most widely used DMARD. <ul style="list-style-type: none"> • Pregnancy: ❖ Women should avoid pregnancy for at least 3 months after treatment has stopped BNF also advises that men using methotrexate need to use effective contraception for at least 3 months after treatment. <ul style="list-style-type: none"> • Prescribing methotrexate: ❖ Methotrexate is taken weekly, rather than daily. ❖ Check CBC, RFTS & LFTS before starting treatment and repeated weekly until t stabilized, thereafter patients should be monitored every 2-3 months therapy. ❖ Folic acid 5mg once weekly should be co-prescribed, taken more than 24 hours after ❖ methotrexate dose ❖ The starting dose of methotrexate is 7.5 mg weekly (source: BNF) ❖ Avoid prescribing trimethoprim or Cotrimoxazole concurrently→ Increases risk of marrow aplasia <ul style="list-style-type: none"> • Sulfasalazine • Leflunomide • Hydroxychloroquine <ul style="list-style-type: none"> ○ TNF-inhibitors: (can cause Drug induced lupus) ❖ The current indication for TNF-inhibitor is an inadequate response to at least 2 DMARDs including methotrexate. ❖ It includes, ❖ Etanercept: (can cause demyelination & reactivation of TB) ❖ Infliximab (risks include reactivation of TB) ❖ Rituximab: <ul style="list-style-type: none"> • Other important treatment options include analgesia, physiotherapy, and surgery.

Extractable Nuclear Antigens

- ❖ Specific nuclear antigens, usually associated with being ANA positive.

anti-Ro	Sjogren's syndrome, SLE, congenital heart block
anti-La	Sjogren's syndrome
anti-Jo 1	Polymyositis
anti-scl-70	Diffuse cutaneous systemic sclerosis
anti-centromere	Limited cutaneous systemic sclerosis

Gout	Pseudogout
❖ Crystal deposition disease, characterized by deposition of monosodium urate crystals into joints and other tissues	❖ Crystal deposition disease, characterized by deposition of calcium pyrophosphate deposition crystals within articular cartilages.
❖ Most common site → 1 st metatarsophalangeal joint (podagra)	❖ Most common site is ankle
❖ Crystals → needle like, negative birefringent	❖ Crystals → rhomboid shape, positive birefringent
❖ Treatment ❖ acute attack → NSAIDs, Colchicine, steroids ❖ Chronic attack → Allopurinol (should not be used in acute attack), Febuxostat	❖ Treatment ❖ NSAIDs, Colchicine, steroids

	<u>Osteomyelitis</u>	<u>Septic arthritis</u>
Definition	❖ Osteomyelitis is an infection of the bone. It normally affects the long bones of the body; however, it can affect any bone	❖ Septic arthritis is an infection of any joint and is an orthopedic emergency. It most commonly affects the hip or knee joint, however it can affect any joint in the body
Features	❖ Subacute onset of limp / non-weight bearing / refusal to use limb. ❖ Localized pain and pain on movement ❖ Tenderness ❖ Soft tissue redness / swelling may not be present & may appear late. ❖ +/- Fever	❖ Acute onset of limp / non-weight bearing / refusal to use limb ❖ Pain on movement and at rest ❖ Limited range / loss of movement ❖ Soft tissue redness / swelling often present. ❖ Fever
Investigations	❖ MRI is gold standard	❖ Urgent joint aspiration for synovial fluid microscopy and culture ❖ Blood cultures
Organisms involved	❖ Most common agent → S. aureus ❖ IV drug users → S. aureus ❖ Neonates → H. influenza ❖ Sickle cell disease → Salmonella	❖ S aureus (Most common) ❖ Streptococcus ❖ Neisseria gonorrhoeae

SERONEGATIVE SPONDYLARTHROSIS (SPONDYLOARTHROPATHIES)

- ❖ **Common features**
 - Associated with HLA-B27
 - Rheumatoid factor negative - hence 'seronegative'
 - Peripheral arthritis, usually asymmetrical
 - Sacroiliitis
 - Enthesitis (inflamed insertion sites of tendons), e.g. Achilles tendonitis, plantar fasciitis
- ❖ Types: (mnemonic: **PAIR**)

Psoriatic Arthritis	<ul style="list-style-type: none"> ❖ Occurs in approximately 10% of patients with psoriasis. ❖ Associated with skin psoriasis and nail lesions. ❖ Asymmetric and patchy involvement ❖ Dactylitis and "pencil-in-cup" deformity of DIP on x-ray
Ankylosing Spondylitis	<ul style="list-style-type: none"> ❖ HLA-B27 association is most striking with this entity (as many as 90% of patients) ❖ This chronic condition affects the spine and sacroiliac. ❖ joints and can lead to rigidity and fixation of the spine as a result of bone fusion (ankylosis)---leading to Bamboo spine (vertebral fusion) ❖ Typically, a young man who presents with lower back pain and stiffness ❖ Can cause restrictive lung disease due to limited chest wall expansion (costovertebral and costosternal ankylosis) ❖ Features: Mnemonic the A's--A for Ankylosing spondylitis <ul style="list-style-type: none"> • Apical fibrosis (CXR) • Anterior uveitis • Aortic regurgitation • Achilles tendonitis • AV node block • Amyloidosis
Inflammatory Bowel Disease	<ul style="list-style-type: none"> ❖ Crohn disease and ulcerative colitis are often associated with spondylarthritis.
Reactive Arthritis or Reiter Syndrome.	<ul style="list-style-type: none"> ❖ Classic triad: (Mnemonic: Can't see, can't pee, can't bend my knee.") <ul style="list-style-type: none"> • Conjunctivitis (Can't see) • Urethritis (can't pee) • Arthritis (can't bend my knee) ❖ Organisms responsible: (Mnemonic: Shy Chics) <ul style="list-style-type: none"> • Shigella • Yersinia • Chlamydia • Campylobacter • Salmonella.

Diseases of Skeletal Muscle

Muscular Dystrophies

Duchenne muscular dystrophy	<ul style="list-style-type: none"> ❖ X-linked disorder typically due to frameshift or nonsense mutations ❖ The cause is a deficiency of dystrophin (Duchenne = Deleted Dystrophin) ❖ It begins with weakness in the proximal muscles of the extremities, commencing at about 1 year of age and progressing to immobilization, wasting, muscle contracture, and death in the early teens, most often due to pneumonia caused by weakness of respiratory muscles. ❖ Pseudohypertrophy of calf muscles due to fibrofatty replacement of muscle. Waddling gait. Patient uses hands to walk ❖ Lab → increased serum CK.
Becker muscular dystrophy	<ul style="list-style-type: none"> ❖ X-linked disorder typically due to non-frameshift deletions in dystrophin gene (partially functional instead of deleted). ❖ Less severe than Duchenne
Myotonic dystrophy	<ul style="list-style-type: none"> ❖ Autosomal dominant ❖ Trinucleotide repeat disorder: CTG (You SEE Tonic Gestures) ❖ Characteristics include a weakness associated with myotonia (inability to relax muscles once contracted). ❖ Associated features Cataracts, Toupee (early balding in men), Gonadal atrophy

	Myasthenia Gravis	Lambert-Eaton Syndrome
Frequency	Most common NMJ disorder	Uncommon
Pathophysiology	Autoantibodies to postsynaptic ACh receptor	Autoantibodies to presynaptic Ca ²⁺ channel → ↓ VACH release
Clinical	Ptosis, diplopia, weakness Worsens with muscle use and recovery on rest. Improvement after edrophonium (Tensilon) test	Proximal muscle weakness, autonomic symptoms (dry mouth, impotence) Improves with muscle use
Associated With	Thymoma, Thymic hyperplasia	Small cell lung cancer
AChE Inhibitor Administration	Reverses symptoms (edrophonium to diagnose, Pyridostigmine to treat)	Minimal effect

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

- ❖ Most common connective tissue disorder, more common in women's It is multisystem inflammatory autoimmune disorder.
- ❖ Classic scenario is like rash, joint pain, and fever, commonly in a female of reproductive age
- ❖ **Two most important lesion frequently asked in exam:**
 - Libman-Sacks Endocarditis (Mnemonic: (LSE in SLE)
 - Nonbacterial, thrombi usually on mitral or aortic valve
 - Lupus nephritis:
 - Glomerular deposition, can be nephritic or nephrotic
 - SLE Renal Complications WHO classification
 - Class 1: normal kidney
 - Class II: mesangial glomerulonephritis
 - Class III: focal (and segmental) proliferative glomerulonephritis
 - Class IV. diffuse proliferative glomerulonephritis-most common and severe form
 - Class V: diffuse membranous glomerulonephritis
 - Class VI: sclerosing glomerulonephritis
- ❖ **SLE and Pregnancy:**
 - Unlike many autoimmune diseases systemic lupus erythematosus (SLE) often becomes worse during pregnancy and the puerperium
 - Neonatal complications include congenital heart block, it is strongly associated with anti-Ro (SSA) antibodies
- ❖ **Common causes of death in SLE:**
 - Cardiovascular disease
 - Infections
 - Renal disease

Findings

Antinuclear antibodies (ANA)	Sensitive not specific
Anti-dsDNA antibodies	Highly specific, poor prognosis (renal disease)
Anti-Smith antibodies	Most specific. not prognostic
Antihistone antibodies	Sensitive for drug-induced lupus (eg, hydralazine, procainamide)
C3.C4	Formation of complexes leads to consumption of complement

Diagnostic criteria (manifestation)

Presence Of 4 Of Following 11 Criteria (mnemonic: DOPAMINE RASH)
Discoïd rash
Oral ulcers
Photosensitivity
Arthritis (non-erosive)
Malar rash (butterfly rash on cheeks and nose with sparing of nasolabial folds)
Immunological→ positive anti-dsDNA (very specific prognostic), anti-Sm (very specific, non prognostic), Antiphospholipid antibodies
Neurological: seizures or psychosis
Renal proteinuria, glomerulonephritis
ANA positive (Best screening test)
Serositis: Pericarditis, Pleuritis
Hematological hemolytic anemia, lymphopenia, leukopenia, thrombocytopenia

Treatment: NSAIDs, steroids, immunosuppressants, hydroxychloroquine

SYSTEMIC SCLEROSIS (SCLERODERMA)

Introduction	<ul style="list-style-type: none">❖ Systemic sclerosis is a generalized disorder of connective tissues of unknown etiology affecting skin, internal organs, and vasculature.❖ More common in females❖ Definitions:<ul style="list-style-type: none">• Scleroderma presence of tight, thickened skin.• Systemic sclerosis Scleroderma + internal organ involvement															
Clinical features	<ul style="list-style-type: none">❖ Skin:<ul style="list-style-type: none">• Tightening and thickening of skin• Mouse-like facies and purse string mouth• Sclerodactyly (claw-like appearance of the hand)❖ Gastrointestinal<ul style="list-style-type: none">• Dysphagia, gastric outlet obstruction, erosive esophagitis❖ Pulmonary (Major cause of mortality and morbidity):<ul style="list-style-type: none">• Pulmonary HTN, pulmonary fibrosis❖ Renal:<ul style="list-style-type: none">• Hypertensive renal crisis characterized by acute onset malignant HTN and renal failure.❖ Miscellaneous:<ul style="list-style-type: none">• Raynaud’s phenomenon, Amenorrhea and infertility															
Types	<div>2 major types</div> <table><tr><th>Limited cutaneous systemic sclerosis</th><th>Diffuse cutaneous systemic sclerosis</th></tr><tr><td>❖ More common (70% cases)</td><td>❖ Less common (30% cases)</td></tr><tr><td>❖ Skin thickening on distal extremities and face only</td><td>❖ Skin thickening on distal extremities, face, and trunk</td></tr><tr><td>❖ Pulmonary HTN>> Pulmonary Fibrosis</td><td>❖ Pulmonary Fibrosis>> Pulmonary HTN</td></tr><tr><td>❖ Prognosis good</td><td>❖ Prognosis bad</td></tr><tr><td>❖ Anti-centromere antibodies (60%)</td><td>❖ Anti-scl-70 antibodies (30%)</td></tr><tr><td>❖ CREST syndrome: i.e.<ul style="list-style-type: none">• Calcinosis.• Raynaud phenomenon• Esophageal dysmotility• Sclerodactyly• Telangiectasia</td><td>❖ Raynaud's phenomenon</td></tr></table>		Limited cutaneous systemic sclerosis	Diffuse cutaneous systemic sclerosis	❖ More common (70% cases)	❖ Less common (30% cases)	❖ Skin thickening on distal extremities and face only	❖ Skin thickening on distal extremities, face, and trunk	❖ Pulmonary HTN>> Pulmonary Fibrosis	❖ Pulmonary Fibrosis>> Pulmonary HTN	❖ Prognosis good	❖ Prognosis bad	❖ Anti-centromere antibodies (60%)	❖ Anti-scl-70 antibodies (30%)	❖ CREST syndrome: i.e. <ul style="list-style-type: none">• Calcinosis.• Raynaud phenomenon• Esophageal dysmotility• Sclerodactyly• Telangiectasia	❖ Raynaud's phenomenon
Limited cutaneous systemic sclerosis	Diffuse cutaneous systemic sclerosis															
❖ More common (70% cases)	❖ Less common (30% cases)															
❖ Skin thickening on distal extremities and face only	❖ Skin thickening on distal extremities, face, and trunk															
❖ Pulmonary HTN>> Pulmonary Fibrosis	❖ Pulmonary Fibrosis>> Pulmonary HTN															
❖ Prognosis good	❖ Prognosis bad															
❖ Anti-centromere antibodies (60%)	❖ Anti-scl-70 antibodies (30%)															
❖ CREST syndrome: i.e. <ul style="list-style-type: none">• Calcinosis.• Raynaud phenomenon• Esophageal dysmotility• Sclerodactyly• Telangiectasia	❖ Raynaud's phenomenon															
Treatment	<ul style="list-style-type: none">❖ NSAIDS, steroids❖ Pulmonary fibrosis= cyclophosphamide❖ Pulmonary HTN= bosentan (endothelin-1 antagonists). HTN renal crisis= ACE inhibitors															

INFLAMMATORY MYOPATHIES (POLYMYOSITIS / DERMATOMYOSITIS)

Overview	<ul style="list-style-type: none"> ❖ Inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions. ❖ May be idiopathic or associated with connective tissue disorders or underlying malignancy (found in 20-25% - more if old patient) ❖ More common in females ❖ Polymyositis is a variant of the disease where skin manifestations are not prominent
Clinical features	<ul style="list-style-type: none"> ❖ Dermatomyositis and polymyositis have the same clinical features except that skin is not involved in Polymyositis. ❖ <u>Features-skin features only in Dermatomyositis.</u> <ul style="list-style-type: none"> ▪ Photosensitive ▪ Macular rash (like SLE) ▪ Heliotrope rash (erythematous periorbital rash) ▪ Gottron's papules - roughened red papules over extensor surfaces of fingers especially on knuckles ▪ Shawl sign- (erythema of face, neck, shoulders and back) ❖ <u>Features -- In both dermatomyositis and polymyositis.</u> <ul style="list-style-type: none"> ▪ Proximal muscle weakness +/- tenderness ▪ Raynaud's ▪ Respiratory muscle weakness ▪ Interstitial lung disease: e.g., Fibrosing alveolitis or organizing pneumonia Dysphagia, dysphonia
Investigations (same in both)	<ul style="list-style-type: none"> ❖ ↑ CK ❖ ANA ⊕ ❖ anti-Jo-1 ⊕ ❖ anti-SRP (signal recognition peptide) ⊕ ❖ anti-Mi-2 antibodies ⊕. ❖ Muscle biopsy-most accurate investigation ❖ Screen for malignancy by U/S abdomen + pelvis- (♀)/+PSA (♂) ❖ CT chest might be needed
Treatment	<ul style="list-style-type: none"> ❖ Steroids followed by long-term immunosuppressant therapy (eg, methotrexate)

SJOGREN SYNDROME

Introduction	<ul style="list-style-type: none"> ❖ Autoimmune disorder characterized by destruction of exocrine glands (especially lacrimal and salivary) by lymphocytic infiltrates. ❖ Predominantly affects women 40-60 years old.
Clinical Manifestation	<ul style="list-style-type: none"> ❖ Triad of <ul style="list-style-type: none"> • Xerostomia (dry mouth). • Keratoconjunctivitis sicca (dry eyes), and one of several • Connective tissue or other autoimmune diseases, most often rheumatoid arthritis ❖ Sicca syndrome is a variant characterized by xerostomia and keratoconjunctivitis alone. ❖ Involvement of salivary glands, (bilaterally enlarged parotids) ❖ Involvement of lacrimal glands
Investigation	<ul style="list-style-type: none"> ❖ ANA ⊕, ❖ Anti SS-A (anti-Ro) less specific ❖ Anti SS-B (anti-La) - Highly specific

HIGH YIELD POINTS + PAST PAPERS BCQs

1. Flat lesion < 1cm size with change in skin color = Macule
2. Superficial most layer of skin = stratum corneum
3. 5 Layers of skin = Come Let's get sun burn → Stratum corneum, lucidum, granulosum, spinosum, basale
4. Location of melanocytes in skin = Stratum Basale
5. Water proofing of skin done by = Keratin
6. Distinctive arrangement of collagen fibers in skin is found in = Reticular layer
7. Reticular fibers are found in = Tonsils > dermis reticular layer
8. Most common ulcer = venous ulcer on gaiter area (medial malleolus).
9. Neuropathic ulcers on bony prominences, no pain, absent reflexes.
10. Curling ulcer is due to inhalational burn. Cushing ulcer by brain injury. Martorell ulcer by hypertension
11. Itchy lesion on genitals and fingers web spaces. Itch more in night = Scabies
12. Incidence of lichen planus = 1-10%. Risk of lichen planus into malignancy = 10-15%
13. Lichen planus association = HCV. Polyarteritis nodosa association = HBV (30%)
14. Premalignant nevus = dysplastic nevus > congenital nevus > compound > intradermal > junctional nevus
15. Most common skin cancer = BCC. Location = upper lip. Most common type of BCC is nodular BCC.
16. BCC shows palisading pattern, pearly nodule with rolled margins. Locally invasive = BCC
17. Slow growing malignant tumor = BCC
18. SCC location = lower lip. Everted margins. SCC arising from skin after burn is called Marjolin's ulcer.
19. Most common type of melanoma = superficial spreading. Risk factor = Sunlight (most imp)
20. Metastasis of melanoma occur by = Vertical growth. Marker of melanoma = S-100
21. Most aggressive cancer is melanoma. Xeroderma pigmentosa is a risk factor also
22. Nodular melanoma on trunk, lentigo on face, acral lentigo on palm & soles.
23. In acanthosis- skin layer affected = Spinosum. After injury, 1st layer to heal = Stratum basale
24. Hairy leukoplakia associated with EBV in HIV
25. Blisters on arm with little skin damage = 2nd degree burn
26. A child has patch on scalp which is leathery. On microscopy, papillomatous projection on epidermis, abundant sebaceous glands on epidermis. Serious complication = basal cell carcinoma. Diagnosis is sebaceous nevus. It can complicate to BCC
27. Premalignant lesion is = dysplastic nevus
28. Common malignancy linked with acanthosis = Gastric adenocarcinoma
29. Lesion on cheeks that needs excision = Actinic keratosis. Most common cause of SCC = Bowen disease
30. Leasur trelat sign seen in = seborrheic keratosis
31. History of 3rd degree burn, stratum corneum, spinosum, lucidum acute loss leads to = acute Water loss
32. A patient having inflamed lesions with clearly demarcated borders on cheeks, nose = Erysipelas
33. A farmer with horn like lesion on forehead = acanthosis
34. Most common premalignant lesion = leukoplakia. Most lethal premalignant lesion = Erythroplakia
35. Most common premalignant condition = Oral submucosal fibrosis
36. Most lethal premalignant condition = Lichen planus
37. Common premalignant lesion in the mouth of adult that may cause cancer = Chronic ulcer
38. Healing of burn starts from which layer = stratum basale / basal layer of epidermis
39. Finger like projection on lid, histology shows epithelial cells. Most likely = Papilloma (finger like projections)
40. Shaft of hair composed of = Cortex of hair
41. Cause of edema in burn patient due to loss of = albumin
42. UV exposure may lead to = Cataract (if no option of skin cancer)
43. Most common cause of death in SLE due to = Renal disease
44. Pencil in cup appearance of DIP on x ray = Psoriatic arthritis
45. HLA-B27 associated with = Ankylosing spondylitis > Uveitis
46. Osteoid osteoma occurs in cortex of bone, has a radiolucent osteoid core
47. Rheumatoid factor is = IgM antibody that targets Fc region of IgG
48. RF is marker of disease activity and tissue damage in RA
49. H/o Knee trauma, chondrocalcinosis on X ray. Rhomboid crystals = Pseudogout

50. Sjogren syndrome associated with = rheumatoid arthritis
51. Osteophytes, Heberden's nodes, bouchards nodes seen in = Osteoarthritis
52. Osteomalacia is due to = inc osteoid maturation time. Main mineral of bone = Calcium hydroxyapatite
53. Inc head size, hearing loss, warm skin, bone pain, seen in = Paget's disease
54. Bilateral parotid enlargement with dry eyes and dry mouth is = Sjogren syndrome
55. Caplan syndrome = RA + pneumoconiosis
56. Most specific for SLE = Anti-smith Ab. Most sensitive for SLE = ANA
57. Diagnostic test for myasthenia gravis = Ach receptor antibodies. Confirmatory/gold standard = EMG
58. Patient with maxillary swelling, On imaging, it appears radiolucent and radio-opaque with ground glass appearance. Diagnosis is = Fibrous dysplasia
59. Bone remodeling is done by = Osteoblast + osteoclast. Bone remodeling vitamin = Vit C
60. Bone mineralization by vit D, while, demineralization by PTH
61. Patient with dry eyes and dry mouth, investigation to be done = Anti SSA
62. Fracture of which part of bone stops longitudinal growth = Epiphyseal plate
63. Child with fever, arthritis, rash and blindness. The diagnosis = chronic juvenile arthritis
64. Osteonic canal running obliquely and transversely connecting the medullary cavity with cortex is called Volkmann canal. Which bone cell has different origin than other = Osteoclast
65. Patient on dialysis develops osteoporosis due to increase osteoclastic activity of = PTH
66. Decrease in complement levels occur in = SLE (low C3, C4). Malar rash seen in SLE
67. Marker of osteoblastic activity = alkaline phosphatase (ALP)
68. Sjogren syndrome patient ANA +Ve, most serious long term complication = Pulmonary interstitial fibrosis
69. Rheumatoid arthritis in pregnancy leads to = mitral stenosis
70. Acute left sided chest pain with tenderness at 5th, 6th ICS = costo-chondritis
71. Bone strength depends on = bone matrix and mineral ratio
72. Most common finding in autoimmune disease = Hematological
73. Defect in SLE = failure of B & T cells tolerance to self-antigen
74. A 25 year old lady presents with fingers turning pale in cold, tight skin with mild enlarged spleen, urea and creatinine, ANA +Ve. Diagnosis is = Scleroderma (systemic sclerosis)
75. Anti-jo antibodies +ve, most likely finding = Skin rash (Dermatomyositis)
76. Astronaut in space for very long time is at risk to develop = decreased bone mass
77. 35 year old female with hematuria, proteinuria in urinalysis, cachexic look. Most likely = lupus nephritis
78. Most common bone tumor in 2nd decade of life = Osteosarcoma- involves metaphysis
79. Route of osteomyelitis = through metaphysis, hematogenous spread.
80. Young lady with h/o recurrent abortion and thrombosis = anti-phospholipid antibody syndrome
81. Bone forming cells are osteoblasts. Mature bone cells are osteocytes
82. Old man develops fever, pain raised TLC, synovial culture -Ve. Likely condition = acute Gout
83. Diabetic lady with morning stiffness > 1 hour is suffering from = Rheumatoid arthritis
84. SLE affects mostly = Joints (arthritis)
85. Tumor having multinucleated giant cells and stromal cells on histology. On X ray, finding = Soap bubble lesion (Giant cell tumor- involves epiphysis)
86. Child with retinoblastoma will have risk of = osteosarcoma. Rb gene involved.
87. Specific diagnosis of gout is by = Monosodium urate (MSU) crystals in joints, -Ve birefringent-needle shaped
88. Cause of osteoporosis in 60 year old lady = Hormonal insufficiency/endocrinological disturbance
89. Patient on chronic steroid therapy will be at risk of = osteoporosis and fractures
90. Metabolic respond to trauma, skeletal muscles respond by = Inc proteolysis
91. A 50 years old man is awakened in the middle of the night with acute pain & tenderness of the right knee. He has a low grade fever. His knee is hot, tender & swollen. Analysis of fluid from right knee shows: leukocytes 70,000/mm³ with 75% neutrophils, crystal analysis = negative birefringent, gram stain = negative. The most likely diagnosis is = Gout. TLC can be > 50,000/mm³ in acute gout

CELLULAR ADAPTATIONS & CELL INJURY

CELLULAR ADAPTATIONS	Cellular responses in reaction or response to Stress - may be Physiological or Pathological. 4 Basic Mechanisms of Adaptation are: Hypertrophy, Hyperplasia, Metaplasia, Atrophy.
HYPERTROPHY	<ul style="list-style-type: none"> ○ increase in the size of cell leading to increase in size or Volume of Organ ○ Inc structural proteins & Organelles is the mechanism. ○ It is reversible change or adaptation. May be Physiological/Pathological <p><u>Examples</u></p> <ul style="list-style-type: none"> ➤ Cardiac Hypertrophy in HTN (LVH), Breast enlargement, Skeletal muscle Hypertrophy
HYPERPLASIA	<ul style="list-style-type: none"> ○ Inc in the Number of cells leading to increase in Size or Volume of the Organ ○ Controlled proliferation of stem cells and differentiated cells. ○ It is reversible. ○ May be Physiological or Pathological and can lead to Dysplasia and cancer. <p><u>Examples</u></p> <ul style="list-style-type: none"> ➤ Benign prostatic hyperplasia ➤ Uterus and breast enlargement in pregnancy ➤ Compensatory hyperplasia in Liver and kidney after resection of a part ➤ Mechanism of Fibroids formation is Hyperplasia
METAPLASIA	<ul style="list-style-type: none"> ○ One Cell Type changes to another type of cell (e.g., Epithelium change) ○ May also occur in Connective tissue. ○ Mechanism: Reprogramming of Stem cells due to chronic irritation > Inflammation, infection ○ The new cell type can adapt better to the stressors. It is a reversible change. ○ It may progress to Dysplasia and carcinoma if the stressor or stimuli is persistent (for years) <p><u>Examples</u></p> <ul style="list-style-type: none"> ➤ In Smokers – Change of Respiratory epithelium (Pseudostratified) to Stratified Squamous. ➤ In GERD – Squamous epithelium of oesophagus changes to Simple Columnar with goblet cells (intestinal type) ➤ Metaplasia of connective tissue can also occur (Formation of bone within muscle after trauma known as myositis Ossificans) A Mass or Lump is felt after trauma e.g., in Arm or thigh. ➤ Vit A def may led to metaplasia. ➤ Vagina adenosis -- metaplasia ➤ Endo cervix epithelium covered by Squamous epithelium is Metaplasia.
ATROPHY	<ul style="list-style-type: none"> ○ Decrease in the size of Organ or dec in tissue mass. It is reversible phenomena. ○ Dec in Actin & Myosin or Cytoskeletal elements degradation is the mechanism. ○ Dec protein synthesis occurs. ○ Dec No. of cells (apoptosis) and Aging process involves atrophy. <p><u>Examples</u></p> <ul style="list-style-type: none"> ➤ Atrophy of disuse ➤ Limb placed in a cast after fracture leading to pressure atrophy via dec actin & Myosin. ➤ Denervation atrophy ➤ Loss of blood supply ➤ Decreased Workload
DYSPLASIA	<ul style="list-style-type: none"> ○ change in shape, size / uniformity of cells i.e., pleomorphism due to chronic irritation / infection. ○ abnormal mitosis is seen though not a true adaptive response. ○ it is a disordered pre-cancerous growth. ○ Characterized by loss of polarity and change in size or shape of cells. ○ Mild to moderate dysplasia is reversible. ○ severe dysplasia → carcinoma in situ to cancer <p><u>Examples</u></p> <ul style="list-style-type: none"> ➤ cervical intraepithelial neoplasia CIN I, CIN II, CIN III ➤ Actinic Keratosis

Key Facts – Cellular Adaptations

- Change in cell size, shape or Polarity is dysplasia. Dysplasia is recognized by these features.
- Change in Cell type is Metaplasia.
- Hyperplasia & Hypertrophy may occur together e.g., Uterus in pregnancy.
- Brain doesn't undergo Metaplastic change. May undergo Atrophy e.g., in Alzheimer's disease.
- Starvation may cause atrophy of all except Brain.
- Hoarseness of voice in laryngeal nodule is due to: Hyperplasia > Hypertrophy.
- Lipofuscin indicates Brown atrophy > Autophagy > Atrophy.
- Epithelium metaplasia is reversible and Mesenchymal metaplasia is Irreversible.
- Vaginal Adenosis is a type of metaplasia. Lobular Hyperplasia occurs in Lactating mother.
- Cellular Vault is maintained via Transport of mRNA > Apoptosis.

ABNORMALITIES OF DEVELOPMENT

ABNORMALITIES OF DEVELOPMENT	
Agenesis	Absent organ due to absent primordial tissue
Aplasia	Absent organ despite present primordial tissue > Failure of cell production
Hypoplasia	incomplete organ development, Primordial tissue present. The cause is the Decreases in cell production during embryogenesis that may Result in relatively small organ e.g., Streak ovary in turner syndrome
Malformation	Intrinsic disruption, occur during the embryonic period (weeks 3-8)
Deformation	Extrinsic disruption, occurs after the embryonic period

CELL INJURY

- Most common cause of cell injury is **Hypoxia**. Ischemia is the MCC of Hypoxia.
- Other causes of cell injury include Toxins, Physical agents, radiations, Genetic, infections e.g., Viruses etc.

Reversible Cell Injury**1. Cellular Swelling:**

Earliest Sign of cell injury

Most likely sign + Most Prominent sign of reversible injury
Swelling is due to Due to Surrounding ECF water entry into the cell because of failure of Na/k+ ATPase & Ca+ pump.

2. Fatty Change**3. Small amorphous densities in Mitochondria**
Earliest Organelle effected is Mitochondria.

4. Mitochondrial swelling & ER Swelling
5. ER Swelling → 1st Ultrastructural change.
6. Dec Glycogen and protein synthesis
7. Chromatin clumping, Plasma membrane blebs
8. Aggregation of peroxidized lipids → Myelin figures

Note:

Mitochondrial Shrinkage is not a Manifestation of cell injury.
It is the Mitochondrial swelling that occurs here.
After Cellular Swelling Mitochondrial swelling is an important event in reversible cell injury.

Irreversible Cell Injury

1. **Cell membrane rupture** is the surest sign and hall mark of irreversible cell injury.
2. Massive Calcium influx → most imp earliest event or earliest reliable sign of irreversible injury
3. **Large amorphous densities in mitochondria**
4. Myelin figures (more Prominent here)
5. Mitochondrial dysfunction, not shrinkage
6. Nuclear degradation occurs as follows.

Pyknosis	Nuclear condensation - Inc in Basophilia
Karyorrhexis	Nuclear Fragmentation
Karyolysis	Nuclear dissolution Loss of Basophilia due to DNA loss

Remember -- Sequence for Surest/ reliable sign of irreversible injury.
Membrane rupture > Lysosomal rupture > Massive CA influx
(Ca+ influx - earliest imp event)
Apoptosis & necrosis are two important mechanisms of irreversible injury causing cell death

CELL DEATH

Feature	Apoptosis	Necrosis
Definition	Programmed cell death using ATP	Cell death along with degradation of tissues by hydrolytic enzymes
Causes	Physiological and pathological processes	Hypoxia, toxins
Morphology	No inflammation, death of single cells Cell membrane remains intact. Cell shrinkage, cytoplasmic blebs on membrane Apoptotic bodies, chromatin condensation Phagocytosis of apoptotic bodies by macrophages	Inflammation present, death of group of cells Cell swelling with membrane disruption. Damaged organelles, nuclear disruption Phagocytosis of cell debris by macrophages
Molecular changes	Lysosomes and other organelles intact Genetic activation by proto-oncogenes and onco-suppressor genes, cytotoxic T cell mediated targeted killing	Lysosomes breakdown with liberation of hydrolytic enzymes Cell death by ATP depletion, membrane damage and free radical injury

APOPTOSIS	<ul style="list-style-type: none"> ATP-Dependant process, Cell Membrane Remains intact with Deeply Eosinophilic Cytoplasm + Basophilic Nucleus DNA Laddering/Step Ladder pattern on Gel electrophoresis is sensitive indicator of apoptosis (TUNEL +Ve) Apoptotic bodies formed are the result of DNA Fragmentation into small size particles. Most characteristic feature of Apoptosis is Pyknosis. Most imp Event is the Activation of Caspases. Initiator Caspases: Caspase 8, 9 Executioner Caspases: Caspases 3, 6, 7. Caspase 3 is most imp effector caspase. Pro-Apoptotic Factors: BAX, BAK, P53 Anti-Apoptotic Factors: BCL-2, BCL – XL (Remember it by: 2XL) Bcl – 2 Over Expression relates to Cancer e.g., Follicular Lymphoma by decreasing Caspases. Pathways Of Apoptosis: 1. Intrinsic (Mitochondrial) Pathway. 2. Extrinsic Death Receptor
Intrinsic mitochondrial pathway	<p>Activates Caspase 9, Regulated by BCL 2 family → BAX, BAK, P53 (Pro-apoptotic) while BCL – 2, BCL -XL (Anti-apoptotic)</p> <p>Examples: DNA damage (radiation, toxins, or ROS), hypoxias Misfolded proteins are removed by this pathway. Also involved in Embryogenesis.</p>
Extrinsic death receptor pathway	<ul style="list-style-type: none"> Activates Caspases 8 (E for eight and extrinsic) Initiated by Fas -Fas Ligand interaction or TNF receptor interaction. Cytotoxic T cell release of Perforin and Granzyme B involved. Fas – Fas Ligand interaction is Important in Thymic Medullary Negative Selection
Physiological apoptosis	<ul style="list-style-type: none"> During Embryogenesis and Thymic Involution Shedding of Endometrium & GIT Epithelium Regression of Lactating Breasts Post – inflammatory Apoptosis of Neutrophils and Lymphocytes
Pathological apoptosis	<ul style="list-style-type: none"> Anti-cancer drugs induced cell death, Cytotoxic cell death in Hep B, C or viral infections. Cell death in MI, Alzheimer's disease. CD4+ depletion in AIDS. DNA damage due to (Radiations, toxins, ROS), Hypoxia, Misfolded proteins. Pathological atrophy (Prostate Atrophy after Orchidectomy).

NECROSIS	<ul style="list-style-type: none"> Pathological process involving death of group of cells, independent of ATP, inflammation present. Cytoplasm: Eosinophilia, glossy appearance, Vacuolated Nuclear changes: Pyknosis, Karyorrhexis, Karyolysis Six Morphological Patterns of Necrosis are as follows:
Type	Features
Coagulative necrosis	Seen in solid organs like Liver, kidney, Heart except Brain Associated with hypoxia, ischemia, or infarction. Cellular outline remains preserved with loss of nuclei
Liquefactive necrosis	Seen in infection, pus or abscess and ischemic Brain injury. Enzymatic digestion of cells with abscess formation is the pathological basis for it
Caseous necrosis	Cheese like appearance of necrotic tissue e.g., in Tb It is a mixture of Coagulative + Liquefactive necrosis
Fat necrosis	Occurs in Omentum, pancreas and breast (traumatic) due to the action of lipase on fatty tissue. For example, in acute pancreatitis, trauma to breast and after GI surgery
Fibrinoid necrosis	Due to antigen -antibody complexes deposition in the wall of vessels leading to fibrin leakage. Examples: Polyarteritis nodosa, malignant hypertension, Aschoff bodies in rheumatic heart disease
Gangrene	Necrosis with superadded putrefaction Dry gangrene resembles coagulative necrosis while wet gangrene resembles liquefactive pattern. In dry gangrene, there is a distinct boundary of necrotic tissue with surrounding healthy tissue. In wet gangrene, there is no specific boundary, and it is infected e.g., Diabetic foot

- Pyroptosis** is the Caspases – 1 dependant programmed cell death that is inflammatory in nature in response to intracellular pathogens e.g., some viral infections.
- Necroptosis** is Programmed type of necrosis. Apoptosis + Necrosis = Necroptosis

	Dry Gangrene	Wet Gangrene
Site	Lower limbs commonly	Bowel (GIT)
Mechanism	Arterial occlusion	Venous occlusion
Gross	Organ is dry, shrunken, and black	Moist, soft, swollen, and dark
Demarcation	Line of demarcation present	No line of demarcation
Bacteria	Bacteria fail to survive	Numerous bacteria present
Prognosis	Better due to little septicaemia	Poor due to profound toxemia

Key Facts – Apoptosis & Necrosis

- Basophilia of cell is due to ribosomes > RER.
- eosinophilia of cell is due to loss of RNA or loss of cytoplasmic RNA.
- there is no inflammation or membrane disruption in apoptosis.
- sex steroids inhibit apoptosis whereas cortisol increases apoptosis.
- councilman bodies are present in apoptosis (prefer yellow fever).
- Piecemeal necrosis is seen in Acute on Chronic (Chronic active Hepatitis).
- Solid organs like Heart, Liver & Kidney show Coagulative pattern.
- Infections (Pus / Abscess) depict Liquefactive pattern.
- Fat necrosis may be Enzymatic (Acute Pancreatitis) or Traumatic (e.g., Trauma to Breast → Fat necrosis).
- Fibrin material is deposited in wall of arteries in Fibrinoid necrosis, seen in Polyarteritis nodosa.
- Most common complication of Diabetes: Dry Gangrene → also most common Gangrene in DM.
- Diabetic Foot is an example of Wet Gangrene.
- Diabetes with complication → Prefer Dry Gangrene > Wet gangrene.
- Caseous necrosis = Coagulative + Liquefactive necrosis.

OXYGEN DEPRIVATION

ANOXIA	Anoxia is the consequences of complete lack of Oxygen.										
HYPOXIA	<p>decreased Oxygen supply to the tissues → Oxidative Phosphorylation stops. Build of Lactic acid (Low PH) and Metabolic acidosis. Cause are Anaemia, CO Poisoning, Hypoxemia.</p> <p>The most common Physiological cause is Hypoventilation and Pathological cause is Ischemia.</p> <p>Types: Mnemonics: HASH → Hypoxic Hypoxia, Anaemic, Stagnant, Histotoxic.</p> <table border="1"> <thead> <tr> <th>Type</th><th>Features and Examples</th></tr> </thead> <tbody> <tr> <td>Hypoxic</td><td>Due to low O2 tension e.g., in high altitude, hypoventilation and V/Q mismatch.</td></tr> <tr> <td>Anemic</td><td>Due to low O2 carrying capacity e.g., in Anemia (blood loss), CO2 poisoning.</td></tr> <tr> <td>Stagnant</td><td>Due to low perfusion in shock, heart failure or ischemia.</td></tr> <tr> <td>Histotoxic</td><td>Due to decreased cellular respiration i.e., unable to use O2 e.g., in cyanide poisoning.</td></tr> </tbody> </table>	Type	Features and Examples	Hypoxic	Due to low O2 tension e.g., in high altitude, hypoventilation and V/Q mismatch.	Anemic	Due to low O2 carrying capacity e.g., in Anemia (blood loss), CO2 poisoning.	Stagnant	Due to low perfusion in shock, heart failure or ischemia.	Histotoxic	Due to decreased cellular respiration i.e., unable to use O2 e.g., in cyanide poisoning.
Type	Features and Examples										
Hypoxic	Due to low O2 tension e.g., in high altitude, hypoventilation and V/Q mismatch.										
Anemic	Due to low O2 carrying capacity e.g., in Anemia (blood loss), CO2 poisoning.										
Stagnant	Due to low perfusion in shock, heart failure or ischemia.										
Histotoxic	Due to decreased cellular respiration i.e., unable to use O2 e.g., in cyanide poisoning.										
HYPOXEMIA	Decreased Blood O2 (low Partial pressure of O2 in blood) regardless of the cause < 80mmhg, can be measured by Pulse Oximeter. Causes include high altitude and hypoventilation. A – a gradient increases										
ISCHEMIA	insufficient blood flow to cells or Organs that to maintain their normal function due to impaired arterial flow or impaired Venous drainage										
ASPHYXIA	inadequate tissue perfusion which fails to meet metabolic demands of tissues for oxygen and waste removal.										

Key Facts

- Arterial PO2 remains same in CO Poisoning.
- Arterial PCO2 increase in Hypoxic Hypoxia.
- Venous O2 increase in Histotoxic Hypoxia.
- O2 therapy is successful in Hypoxic Hypoxia.
- O2 therapy is NOT helpful in Stagnant or Anaemic Hypoxia.
- CO has 250 times more affinity than O2 for Hb.
- Cellular respiration or metabolism is affected in Histotoxic hypoxia.

INFARCTION	<p>Localized area of ischemic necrosis in an organ or Tissue resulting most often from reduction of arterial blood Supply or occasionally its venous drainage</p> <p>Vessel obstruction → Ischemia → Hypoxia → Reduced O2 → Thrombus formation → Necrosis → Infarction.</p> <p><u>Factors</u> that influence infarct development are: Anatomy of vascular supply, Rate of occlusion, Tissue susceptibility to hypoxia and Hypoxemia</p>
Type	Features
Haemorrhagic or Red infarct	<ul style="list-style-type: none"> ○ Caused by artery or vein occlusion (or Reperfusion) seen in soft organs having loose tissue e.g., brain, liver, lungs, and GIT. ○ These organs typically have dual blood Circulation. Loose texture tissue allows RBC release from damaged vessels that will flood the Necrotic tissue and infarct will appear red. ○ Infarct grossly appear as wedged shape. ○ Apex of lesion is towards blood vessel, base toward the surface
Anaemic or White (Pale) infarct	<ul style="list-style-type: none"> ○ caused by arterial occlusion and observed in solid organs such as heart, kidney, and spleen. ○ Include single blood supply and referred as 'white' → lack of haemorrhage and limited RBC. ○ Infarct grossly appear as wedged shape area of necrosis with haemorrhage border zone.

Key Facts – Infarction

- Neurons are Most Sensitive to Hypoxia i.e., undergo irreversible damage in 3 – 5 minutes - most prone to damage are Hippocampal neurons + Purkinje cells of Cerebellum.
- Myocardial cells are also extremely prone to Hypoxia and ischemic infarction.
- Fibroblasts are Least sensitive or Most Resistant to hypoxia.
- Liver is most Resistant to Develop infarction (Least chances of Infarction in liver).
- White infarct seen in Heart/Kidney, while red infarct in GIT, Lungs, Liver, Testes, Ovaries.
- **Areas most prone to infarction:**
PCT (straight segment) of Kidney, Sub endocardium of LV in Heart, Zone III of Liver around Central vein, Water shed areas (Splenic flexure, Rectosigmoid junction, ACA/MCA/PCA Boundary areas).
- Ischemia in DM is due to Endarteritis Obliterans.
- endarteritis Obliterans is closely related to -- Syphilitic aneurysm.

CALCIFICATION	<ul style="list-style-type: none"> ○ Deposition of Calcium in tissues giving deeply basophilic (blue) appearance. ○ Calcium can deposit in the Joints, tendons, soft tissues, Viscera's as well as in Malignancy. ○ Morphologically: Two distinct types are seen → 1. Dystrophic 2. Metastatic calcification.
Type	Findings
Dystrophic calcification	<ul style="list-style-type: none"> ○ Deposition of Ca salts in dead and degenerated tissues with normal serum Ca²⁺ levels and metabolism. ○ Causes include necrosis, infarcts, thrombi, hematomas, dead parasites, old scars, atheroma's. ○ It is also seen in psammoma bodies and Tuberculosis.
Metastatic calcification	<ul style="list-style-type: none"> • Deposition of Ca salts in normal tissues in hypercalcemia with deranged Ca metabolism. • Causes: Hyperparathyroidism, Hypervitaminosis D, prolonged immobilization, milk alkali syndrome. • High PH at certain sites favours it e.g., Lungs, stomach, blood vessels and cornea. • Most common sites are Lungs (alveolar septa) > Kidney (basement membrane) • Hyperparathyroidism & Hypoparathyroidism both can lead to Metastatic calcification. • Prefer Hyperparathyroidism > Hypervitaminosis D > Hypoparathyroidism. • Nephrocalcinosis may be seen in Metastatic calcification. • Serum Calcium levels are normal in Dystrophic type, High in Metastatic type

INTRACELLULAR ACCUMULATIONS

They may be normal cellular constituents, abnormal substances, and pigments.

Normal cellular Constituents	Water, proteins, lipids, carbs (glycogen) and calcium etc.
Abnormal substances	May be endogenous and exogenous. Endogenous: products of abnormal synthesis/metabolism e.g., lysosomal diseases. Exogenous: Minerals, carbon, lead, infectious agents (viruses).
Pigments (impart colour)	Exogenous: Carbon, Lead, Tattoos (Cinnabar imparts red colour). Endogenous: Lipofuscin, Hemosiderin, Melanin, Bilirubin (yellow), biliverdin -green.

Carbon	<ul style="list-style-type: none"> • Most common pigment to be accumulated. • Carbon is the ubiquitous air pollutant of urban Life. Picked up by alveolar macrophages Through lymphatic channels to regional (Hilar)Lymph nodes. • Causes blackening of the tissues of lung (Anthracosis). • Anthracosis + fibroblastic reaction = Coal Workers pneumoconiosis.
Lipofuscin	<p>An insoluble yellowish-brown Wear and tear pigment.</p> <p>Lipochrome: Polymer of lipids & phospholipids Complex with protein and derived through lipid peroxidation of polyunsaturated lipids of subcellular membrane.</p> <ul style="list-style-type: none"> • Yellowish brown, finely granular, cytoplasmic (perinuclear) pigment Seen in cells undergoing slow regressive changes in Liver & heart of aging patients. • Lipofuscin indicates: Brown atrophy > Autophagy. If both options not given, then choose Apoptosis.
Hemosiderin	<ul style="list-style-type: none"> • Hb-derived golden yellow to brown granular or crystalline pigment.

	<ul style="list-style-type: none"> • Normal Fe storage form is Ferritin while Excess of iron is stored as insoluble Hemosiderin. • Iron transport via transferrin. Iron + apoferritin = Ferritin micelles. • Local excess (Common Bruises) leads to Hemosiderin deposition. • Heme → Biliverdin → Bilirubin. • Systemic Fe excess or accumulation with no systemic manifestation is known as Hemosiderosis. • Excessive Fe deposition along with systemic features = Hemochromatosis • Fe can be Oxidised by Potassium Ferrocyanide giving Blue Colour with Prussian stain
Melanin	<ul style="list-style-type: none"> • Endogenous, non-haemoglobin derived brown, black pigment. • Tyrosinase catalyses oxidation of tyrosine in melanocytes • it is the only endogenous brown, black pigment. Ochronotic is rare disorder seen in alkaptonuria in which Black pigment deposits in skin, connective tissues, cartilage, etc.

AMYLOIDOSIS

Deposition of Abnormal Proteins (of Beta Pleated Sheet Configuration) in tissues that interferes with organ functioning.

Basically, a disorder of Abnormal protein Folding from Normal Alpha helix configuration into abnormal Beta pleated sheet.

1. **Systemic Amyloidosis** (may be primary 1°), Secondary (2°) or Dialysis associated (beta 2 micro-globulin)
2. **Localized**: Alzheimer's disease, Type 2 DM, Isolated atrial amyloidosis, Senile, Medullary thyroid cancer
3. **Hereditary**: Familial amyloid cardiopathy & Neuropathy

Classification has been given as in table below.

Amyloid type	Amyloid protein	Organ system
AL (Primary)	Monoclonal kappa/lambda chains	Renal, cardiac, GIT, neuro, skin, liver
AA (secondary) a/w chronic illness	Serum Amyloid A (SAA)	Rheumatoid arthritis, IBD, chronic illness, malignancies (Colon Cancer)
Hereditary	Mutant transthyretin (TTR)	Neuro, cardiac
Senile systemic	Wild type TTR, ANP	Cardiac, aorta, GIT
Aβ ₂ M dialysis associated	Beta 2 micro-globulin (β ₂ M)	Musculoskeletal, renal
Organ specific	various	Various: CNS, bladder, skin etc

System	Manifestations
Kidney	Secondary amyloidosis more common here than Primary. Common site is Mesangial of glomeruli. Most Common affected organ in amyloidosis is Kidney. Proteinuria (70%), nephrotic syndrome
Heart	involved in systemic amyloidosis mainly. Localised form (Senile cardiac & AANF). In advanced cases-- restrictive cardiomyopathy & Arrhythmias. GROSS : heart enlarged, pale, translucent and waxy. Epicardium, endocardium & valves show tiny nodular deposits of amyloid. MICROSCOPY : Amyloid deposits in and around Coronaries. In primary amyloidosis, deposits of AL are seen around Myocardial fibres in ring like formations (ring fibres). In localised form, deposits are seen in left atrium and Interatrial septum.
GIT	can occur at any place from Mouth to Anus. Macroglossia is a prominent feature → dysphagia. Gastroparesis constipation, malabsorption.
Liver	Initially involves Space of Disse, Hepatocytes are affected. Hepatosplenomegaly may be present.
Neurological	Bowel/bladder dysfunctions, peripheral neuropathies, carpal tunnel syndrome.
Musculoskeletal	Arthralgia, arthritis, shoulder sign, waxy skin, non-itchy papules, raccoon eyes, ecchymoses.
Haematological	Factor X deficiency (2.5% of cases).
Diagnosis of amyloidosis	Biopsy & Congo Red Stain with Polarized Light are Most Imp Methods. 1. Biopsy of affected organ (e.g., Rectal Biopsy) is gold standard. 2. Subcutaneous abdominal fat aspiration is also sensitive method.

3. Stains:

- a. On H & E: Eosinophilic Extracellular homogenous structureless material deposition
- b. Congo Red stain + Polarized Light → Apple Green birefringence is seen (Diagnostic)**
- c. Thioflavin stain: yellow appearance.
- d. Crystal violet + Methyl violet stain: Rose Pink colour of amyloid

HYALINE CHANGE

Intracellular or intercellular alteration that Gives a homogenous, glassy, pink Appearance in routine H&E staining.

It is a Histological term rather than a specific form of injury. it is seen in:

Intracellular accumulation of proteins, Collagenous fibrous tissue in old scars, Vessel wall in long standing hypertension.

CELLULAR AGING

Known changes that contribute to cell aging:	<ul style="list-style-type: none"> Decreased cellular replication. Non-dividing state of cell, the senescence. Telomere shortening or dec activity of telomerase promotes cell aging. Calorie restriction Promotes Longevity.
Accumulation of metabolic and genetic Damage:	<ul style="list-style-type: none"> Cell life span is determined by a balance Between oxidative damage and molecular Response for repair. Ionizing radiation. Mitochondrial dysfunction. Reduction of antioxidant defence mechanism.
Sirtuins (proteins)	<ul style="list-style-type: none"> With Aging there is decline in sirtuin expression and activity in cells. This has detrimental consequences to the organism and is accompanied by increased risk of diseases of aging. Sirtuins regulate life span and spontaneous tumour development. By Calorie restriction, Sirtuins protein increase Longevity via Inc Insulin sensitivity + metabolism and decreased apoptosis.

FREE RADICALS/REACTIVE OXYGEN SPECIES (ROS)

Generation of ROS	<ul style="list-style-type: none"> Normal metabolic processes. Absorption of radiant energy (ultraviolet light, x-rays). During inflammation. Enzymatic metabolism of exogenous chemicals or drugs. Transition metals (iron and copper) donate or accept free electrons during intracellular reactions and catalyse free radical formation. Nitric oxide (NO) generated by endothelial cells, macrophages, neurons, act as a free radical. Phagocytosis, oncogenesis or tumorigenesis or Carcinogenesis, Regeneration of tissue. WBC (e.g., neutrophils, macrophages) oxidative burst. All these processes generate ROS. Oxygen derived: Superoxide anion (O₂), H₂O₂, OH. Nitric oxide: NO, NO₂, NO₃, ONOO (Reactive peroxynitrite anion). CCl₃ derived from CCL₄.
Mechanism of action	<ul style="list-style-type: none"> Lipid peroxidation of membrane (membrane damage). Oxidative modification of protein (misfolding, breakdown). DNA lesion/mutations.
Inactivation	<ul style="list-style-type: none"> Antioxidant: Vitamin A, C, E, Cysteine, Glutathione (most potent). Scavenging Enzyme: Superoxide dismutase, catalase, Glutathione peroxidase. Most potent is glut-thionine overall. Most potent Vitamin acting as antioxidant is Vit E. ❖ Follow this Order: Glutathione > Transferrin > Vit E > Vit C > Vit A Foods acting as Antioxidants: Chocolate > Apple > Orange. H₂O₂ neutralize by: Catalase and Glutathione peroxidase. Superoxide anion (O₂) neutralizes by Superoxide dismutase (SOD).

Key Facts – Free Radicals

- **OH•**: Strongest free radical. The order is: OH > H₂O₂ > HOCL.
- **CCL₄**: may cause Fatty Liver & centrilobular necrosis.
- Super oxide dismutase prevents brain from Free Radical injury.
- Smoking related anti-oxidants are eliminated by Vit C, so Smokers have reduced vit C.
- In pt undergoing dialysis: Vit B6 is deficient.
- cytosol Free radicals are removed via Selenium.
- Ionizing radiations INDIRECTLY cause damage via ROS or free radicals.
- **Fenton reaction**: H₂O₂ + Fe²⁺ → Fe³⁺ + •OH (ROS) + OH⁻ (OR) H₂O₂ via SOD → •OH (ROS) + O₂.
- Smoking related anti-oxidants are eliminated by Vit C, so Smokers have reduced vit C.
- In pt undergoing dialysis: Vit B6 is deficient.
- Vit E: Prevents Lipid Peroxidation and neutralized oxidized LDL.

EFFECTS OF RADIATIONS

Acute Effects	Skin – Desquamation, Blisters, sterility, Nausea, diarrhoea, Vomiting, Mucositis, alopecia, papilledema, seizures, ataxia
Chronic Effects	<p>Skin -- induration + thickening, Pulmonary fibrosis, GI Ulceration or obstruction, Azoospermia, Urethral strictures.</p> <p>Tumours: Papillary thyroid cancer, Osteosarcoma, angiosarcoma, breast, Ovary & Lung Cancers</p> <p>Osteosarcoma > Leukaemia: Strontium- 90</p> <ul style="list-style-type: none"> • Radiations take around more than 10yrs. more developing cancer (especially skin malignancy) • Leukaemia is most commonly associated with radiations.
Key Facts	<ul style="list-style-type: none"> • Most common acute effect of High dose radiations is: Desquamation • Chronic side effect of Radiations: Endarteritis Obliterans • Late Complication or effect of radiations: Lymphoproliferative Disorders (After 10 to 15 yrs.) • Sometimes, Option of Endarteritis obliterans is given while asking for Late complication and Lymphoproliferative in not in Options, then choose Endarteritis Obliterans for Late complication • Most sensitive phase of cell cycle to radiations = M > G₂ • Radiosensitive tumours: Lymphoma > seminoma > Gliomas > Craniopharyngioma • Most radiosensitive cell = lymphocyte (hematopoietic cells) • most radioresistant organ = Vagina • The Most Radiosensitive tissue = Bone Marrow • Ovaries are Most Radiosensitive Gonads, cervix is most radiosensitive in reproductive organs • Intestinal mucosa is the most Radiosensitive Mucosa • Skin is the most Radiosensitive Organ

PAST PAPERS BCQS

1. In Pak: most common cause of cell injury is -- Malnutrition
2. Overall, around the world most common cause of cell injury: hypoxia
3. Ionizing radiations cause cancer via free radicals
4. Molecular mimicry is the mech of apoptosis in auto immune diseases
5. After delivery, uterus regresses by lysosomal action (autophagy)
6. Large mitochondrial densities seen in irreversible injury
7. Nissls substance present in granular er
8. Cell shrinkage is a feature of apoptosis (irreversible injury)
9. Mitochondrial shrinkage is not seen in cell injury
10. Old age pt, golden brown pigment in liver that stains blue with dye: prefer lipofuscin > hemosiderin
11. Dysplasia is recognized by loss of polarity and architecture. pleomorphism is seen in dysplasia
12. After chemotherapy tumour regresses by: apoptosis
13. Caspases activation is most imp in apoptosis
14. Necrosis in abscess / infection or brain: liquefactive pattern
15. Fibrinoid necrosis seen in: polyarteritis nodosa (PAN)
16. Functional and morphological epithelial change seen in: metaplasia
17. Most common acute effect of high dose radiations is: desquamation
18. Chronic side effect of radiations: endarteritis obliterans
19. After trauma, lump formation in thigh or arm: metaplasia (myositis ossificans or Progressive fibrous dysplasia)
20. Cervical polyp with pleomorphic cells & hyperchromatic nuclei: dysplasia
21. Hydropic change or cell swelling is earliest feature of reversible injury
22. Aplasia is absence of organ development > failure of cell production
23. Rigidity after death is due to: loss or depletion of ATP leading to unbroken actin & myosin bridges
24. Size of muscle reduced after cast application: due to decrease actin & myosin
25. p53 when absent or mutated indicates: Increase cell survival, p53 starts apoptosis
26. Myocardial ischemia: coagulative necrosis (in heart contraction band necrosis is seen)
27. Most potent anti-oxidant is: glutathione > vit e > vit c > vit a
28. Enlargement of heart in HTN is example of: hypertrophy (LVH / RVH)
29. Columnar cells 3cm above gastroesophageal junction: metaplasia
30. Gall bladder containing gastric epithelium is metaplasia
31. Gene involvement mech of cell destruction is: apoptosis
32. Respiratory burst has: bactericidal effect i.e., HOCL kills microbes
33. In smokers: mixture of squamous epithelium with patches of pseudostratified columnar is found in airways
34. Ischemia, infarction and infection all cause cell injury via → ROS (free radical formation)
35. Pyknosis is diagnostic feature of dead cell or apoptosis
36. Hyperplasia is the underlying mech of fibroids formation
37. Massive calcium influx is an earliest reliable feature of irreversible injury
38. Cell membrane rupture is hallmark and most imp feature of irreversible injury
39. Free radicals' formation in cell via: mitochondria
40. OH•: strongest free radical. the order is: OH > H₂O₂ > HOCL
41. By calorie restriction, sirtuin protein increase longevity via increase insulin sensitivity + metabolism & dec apoptosis
42. Basophilia of cell is due to: ribosomes > RER
43. Eosinophilia of cell is due to : loss of RNA / loss of cytoplasmic RNA
44. Radiations used in cancer radiotherapy are: x rays
45. M phase > G2 phase most sensitive to radiotherapy
46. S phase sensitive to chemotherapy
47. Cervix is most sensitive to radiations in reproductive organs (vagina – most resistant)
48. Leukaemia due to radiation overall most common cancer
49. Meningioma most common brain tumour due to radiation.
50. Tumour sensitive to radiation: lymphoma > seminoma > glioma > craniopharyngioma.
51. Medulloblastoma is the most radiosensitive malignant tumour of brain.
52. Biopsy of affected organ (e.g., rectal biopsy) is gold standard in amyloidosis

53. Kidney is not commonly involved in primary amyloidosis
54. Lipofuscin indicates brown atrophy > autophagy.
55. Neurons are most sensitive to hypoxia; cardiac cells are most prone to ischemia
56. Deeply eosinophilic cytoplasm & basophilic nucleus seen in apoptosis
57. Foods acting as antioxidants: chocolate > apple > orange
58. Normal iron storage form: ferritin
59. Excess of iron stored in hemosiderin
60. Most common complication of diabetes: dry gangrene → also most common gangrene in dm
61. Diabetic foot is an example of wet gangrene
62. Diabetes with complication: dry gangrene, diabetic foot with complication is wet gangrene
63. Caseous necrosis = coagulative + liquefactive necrosis
64. Dystrophic calcification is seen in psammoma bodies
65. Most common sites for metastatic calcification are; lungs (alveolar septa) > kidney (basement membrane)
66. Most common pigment to be accumulated is carbon
67. Liver is most resistant to develop infarction (least chances of infarction in liver)
68. White infarct seen in heart/kidney red infarct in git, lungs, liver, testes, ovaries.
69. Arterial po2 remains same in co poisoning
70. Arterial pco2 increase in hypoxic hypoxia
71. Venous o2 increase in histotoxic hypoxia
72. Pro-apoptotic factors.: bax, bak , p53
73. Anti-apoptotic factors: bcl-2, bcl – xl (remember it by : 2XL)
74. Chronic irritation > inflammation is the most common cause in metaplasia. The new cell type can adapt better to the stressors.it is reversible.it may progress to dysplasia and carcinoma if the stressor or stimuli is persistent (for years)
75. In smokers – change of respiratory epithelium (Pseudostratified) to stratified squamous
76. In Gerd – squamous epithelium of oesophagus changes to simple columnar with goblet cells (intestinal type)
77. Metaplasia of connective tissue can also occur (e.g., formation of bone within muscle after trauma, known as myositis ossificans)
78. A mass or lump is felt after trauma e.g., in arm or thigh.
79. Vit A def may led to metaplasia also
80. Vagina adenosis is – metaplasia
81. Endo cervix epithelium covered by squamous epithelium is: metaplasia.
82. Compensatory hyperplasia in = liver and kidney after resection of a part
83. Mech of fibroids formation is hyperplasia + hypertrophy > hyperplasia (mostly in exams single options are given related to this question, choose hyperplasia there. metaplasia is wrong
84. Hoarseness of voice in laryngeal nodule is due to: hyperplasia > hypertrophy
85. Dry gangrene – coagulative necrosis, any type of vasculitis: fibrinoid necrosis
86. After partial pancreatectomy: fat necrosis is seen.
87. Resection of gut reveals granulomatous inflammation: type of necrosis is fat necrosis (omental fat necrosis)

INFLAMMATION & REPAIR

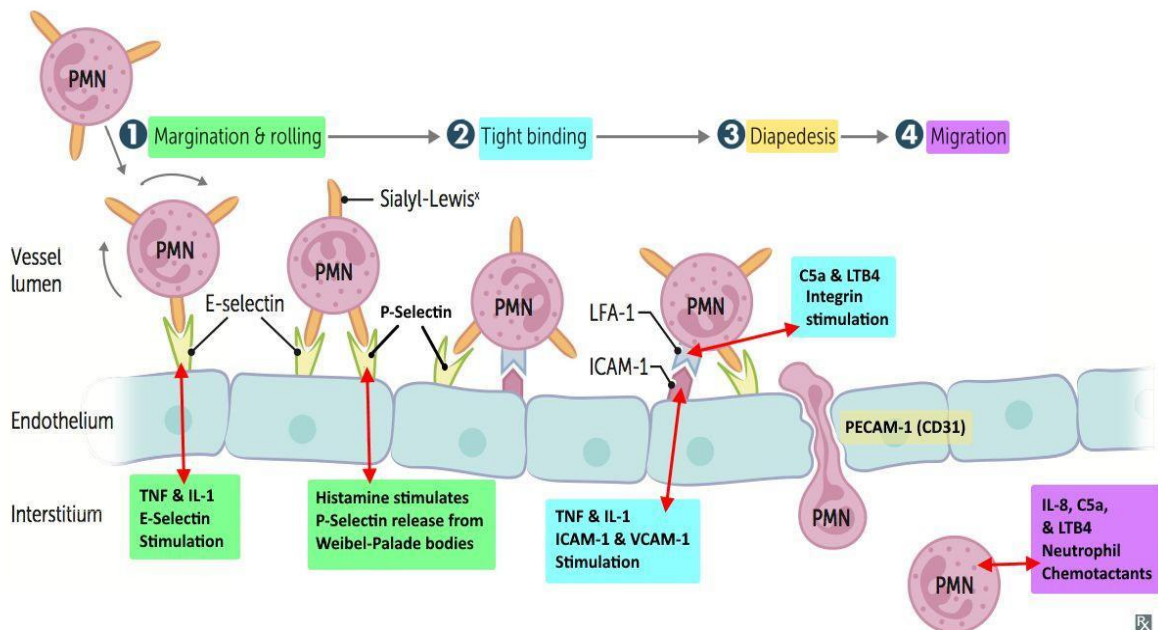
Inflammation	Inflammation is the reaction of vascularized living Tissue to local injury. A series of vascular and Cellular reactions aiming to protect body against the injurious agent.																									
Types	<ol style="list-style-type: none"> Acute: sudden onset and short duration (hours – Days) Chronic: gradual onset and long duration days -Years) <table> <tr> <th></th><th>Acute inflammation</th><th>Chronic inflammation</th></tr> <tr> <td>Cause</td><td>Pathogens, open wounds, harmful stimulation</td><td>Pathogens, allergens, foreign bodies, acute inflammation turned into chronic</td></tr> <tr> <td>Immune cells</td><td>Neutrophils</td><td>Macrophages, lymphocytes, plasma cells, fibroblasts</td></tr> <tr> <td>Mediators</td><td>Histamine, eicosanoids</td><td>Cytokines, growth factors, ROS, hydrolase</td></tr> <tr> <td>Response</td><td>Immediate, fixed</td><td>Delayed, ever changing</td></tr> <tr> <td>Duration</td><td>Few minutes to days</td><td>Few weeks to months or years</td></tr> <tr> <td>Outcomes</td><td>Resolution, pus formation, chronic inflammation</td><td>Tissue damage, tissue fibrosis or necrosis</td></tr> <tr> <td>Features</td><td>Redness, swelling, pain</td><td>Angiogenesis, dry rough scab formation</td></tr> </table>			Acute inflammation	Chronic inflammation	Cause	Pathogens, open wounds, harmful stimulation	Pathogens, allergens, foreign bodies, acute inflammation turned into chronic	Immune cells	Neutrophils	Macrophages, lymphocytes, plasma cells, fibroblasts	Mediators	Histamine, eicosanoids	Cytokines, growth factors, ROS, hydrolase	Response	Immediate, fixed	Delayed, ever changing	Duration	Few minutes to days	Few weeks to months or years	Outcomes	Resolution, pus formation, chronic inflammation	Tissue damage, tissue fibrosis or necrosis	Features	Redness, swelling, pain	Angiogenesis, dry rough scab formation
	Acute inflammation	Chronic inflammation																								
Cause	Pathogens, open wounds, harmful stimulation	Pathogens, allergens, foreign bodies, acute inflammation turned into chronic																								
Immune cells	Neutrophils	Macrophages, lymphocytes, plasma cells, fibroblasts																								
Mediators	Histamine, eicosanoids	Cytokines, growth factors, ROS, hydrolase																								
Response	Immediate, fixed	Delayed, ever changing																								
Duration	Few minutes to days	Few weeks to months or years																								
Outcomes	Resolution, pus formation, chronic inflammation	Tissue damage, tissue fibrosis or necrosis																								
Features	Redness, swelling, pain	Angiogenesis, dry rough scab formation																								

ROLE OF MAJOR CELLS IN INFLAMMATION	
Neutrophils	<ul style="list-style-type: none"> Multilobed nucleus (Bilobed) Neutrophils stain a neutral pink. It is the primary leukocyte in acute inflammation is the major circulating phagocytic cell. Average half of neutrophil in circulation is 6 hours. Infiltrate during the first 6 to 24 hours and are replaced by monocytes in 24 to 48 hours. Pus contains dead neutrophil & microbes. It is responsible for suppuration in abscess. O₂ dependant MPO system is only present in neutrophil and monocytes. Contain enzyme Elastase, nicotine is Neutrophilic elastase inhibitor. Hyper segmented polymorphs (5 or more lobes) are seen in vitamin B12/folate deficiency
Lymphocytes	<p>T Lymphocytes</p> <ul style="list-style-type: none"> 80 % of Lymphocytes, formed in Bone marrow, Mature in Thymus, Anti-tumorigenic (CD8+) Play role in cellular immune response & chronic inflammation. <p>B Lymphocytes</p> <ul style="list-style-type: none"> 20 % of Lymphocytes, Formation, and maturation in Bone marrow Play role in humoral response by Producing Antibodies & Plasma cells, Memory cells. Active against Bacteria & Viruses
Monocytes	<ul style="list-style-type: none"> Large kidney or bean shaped nucleus is characteristic. Extensive “frosted glass” Cytoplasm Monocytes leave the circulation and become macrophages. The half-life is about 1 day, do not reenter into circulation. When monocytes reach the extravascular tissue, they undergo transformation into larger macrophages, which have longer half-lives and a greater capacity for phagocytosis than do monocytes. It is not a phagocytic cell. Monocytes function of granulation tissue is wound healing by second intention in wound contraction
Macrophages	<ul style="list-style-type: none"> The dominant cells of chronic inflammation are tissue cells derived from Circulating blood monocytes after their emigration from the bloodstream. key cells in Chronic inflammation. Macrophages Cause segregation and digestion of foreign bodies. Major Phagocyte in Tissues - Macrophages Major Phagocyte in Circulation or Blood - Neutrophils
Eosinophils	<ul style="list-style-type: none"> Bilobed spectacle shaped nucleus.

	<ul style="list-style-type: none"> Eosinophils are characteristically found in parasitic infections, allergies, and Predominant cell in chronic rhinitis
Basophils	<ul style="list-style-type: none"> Increase in CML and Polycythaemia, decrease in Hodgkin lymphoma. IgE bind on its surface in blood vessel. Dense granules + Ig E. = Basophils IgE is present on Both Basophils + Mast cells Basophilic white blood cells stain dark blue. Eosinophilic white blood cell stain bright red.
Mast cells	<ul style="list-style-type: none"> widely distributed in connective tissues throughout the bod and can participate in both acute and chronic inflammatory responses. IgE-armed mast cells are central players in allergic reactions, including anaphylactic shock Mast cells are abundant in area rich in connective tissue e.g., beneath epithelium Mast cell granules can naturally induce Metachromatic staining

Cardinal signs of acute inflammation	5 Signs <ol style="list-style-type: none"> Rubor – Redness via Histamine mediated vasodilation. Calor - Heat Tumour - Swelling Dolor - Pain (Bradykinin, PGE2) Functio laesa - loss of function
EVENTS in acute inflammation	<ol style="list-style-type: none"> Vascular (transient vasoconstriction followed by vasodilation) Cellular events (MRAT -C; Margination, rolling, adhesion, transmigration, chemotaxis)
VASCULAR events	<ul style="list-style-type: none"> Transient Vasoconstriction (1st step or immediate step) followed by Vasodilation, stasis + increased vascular Permeability via endothelial gap formation and mediators, leading to leakage of fluid out of vessels. Fluid leaked in inflammation is Exudate type dominantly. Mostly affected are Venules i.e., Post capillary Venules.
CELLULAR events	<ul style="list-style-type: none"> Neutrophils are the predominant cells of acute inflammation. Cellular events are as follows; Mnemonics: MRAT - C
Margination	<ul style="list-style-type: none"> first step, process of leukocyte accumulation at the periphery of vessels is called Margination or the displacement of leukocytes by RBC to periphery of vessel or increased No. Of WBCs in Periphery adjacent to endothelium. Slowing, stagnation of the flow occurs due to increased vascular permeability
Rolling	<ul style="list-style-type: none"> slow tumbling and transient adhesion. Leukocytes tumble on the endothelial surface, transiently sticking along the way, by a Process called rolling. This weak and transient adhesions involved in rolling are mediated by the selectin family of adhesion molecules Pave mentation is the Complete Lining up of adhered leukocyte along vessels wall. Rolling or Transient (Weak) adhesion = By Selectins.
Adhesion	<ul style="list-style-type: none"> The next step in the reaction of leukocytes is firm adhesion to endothelial surfaces. Rolling come to stop and adhesion mediated by Integrins expressed on leukocyte cell surfaces interacting with their ligands on endothelial cells. Adhesions Or Firm Adhesion = By Integrins <ul style="list-style-type: none"> ❖ Endothelial: ICAM-1 and VCAM-1. Leukocytes: -LFA-1, mac-1, VLA-4 ❖ ICAM-1 binds LFA-1/ mac-1. VCAM-1 binds VLA-4
Transmigration	<ul style="list-style-type: none"> also called Emigration, Extravasations, Diapedesis Leukocytes migrate through the vessel wall Primarily by squeezing between cells at intercellular junctions (although intracellular. This movement of Leukocytes, called diapedesis, occurs mainly in the postcapillary venules of the systemic Vasculature; it has also been noted in capillaries in the pulmonary circulation. Diapedesis = by PECAM - 31
Chemotaxis	<ul style="list-style-type: none"> After extravasating from the blood, leukocytes migrate toward sites of infection or injury Along a chemical gradient by a process called chemotaxis. Both exogenous and endogenous substances can be chemotactic for leukocytes Chemotaxis implies directed locomotion. Chemo-kinesis: Enhanced random movement Chemotactic factors are IL-8, LTB4, C5a, Kallikrein & Bacterial products.

- Most Potent chemotactic factor is C5a > LTB4.
- But if the Question is regarding potent chemotactic factor produced by the Lipoxygenase pathway? Then it will be LTB4.



MORPHOLOGICAL PATTERNS OF ACUTE INFLAMMATION

Serous	Inflammation with a thin, watery exudate that has an insufficient amount of Fibrinogen to produce fibrin. Examples— blister in second degree burns or Sun burn . viral pleuritis.
Purulent	Purulent (suppurative) inflammation is localized proliferation of pus-forming organisms, such as S. Aureus (e.g., skin Abscesses), acute appendicitis , cellulitis and furunculosis etc.
Fibrinous	Due to increased vessel permeability, with deposition of Fibrin-rich exudate on the surface of the tissue. Commonly occurs on the serosal lining of the pericardium, peritoneum, or pleura.
Pseudomembranous	Seen in Diphtheria & C. difficile infection
Histiocytic	involves Reticuloendothelial system e.g., occurs in Typhoid, Brucellosis, Histoplasmosis
Interstitial	Interstitial or Perivascular in viral infections, Syphilis & arthropod vector diseases (Rocky Mountain fever)

OUTCOMES OF ACUTE INFLAMMATION

Resolution/Healing	by TGF – Beta & IL – 10
Abscess formation	inflammation walled off by fibrosis. Presents with Fever with chills & systemic signs symptoms.
Scarring	Scar formation
Chronic inflammation	If persistent, may turn into chronic form

ACUTE PHASE REACTANTS

Synthesized by liver under influence of IL1, IL6 TNF. They include +Ve and -Ve acute phase reactants

Positive reactants	Levels raised in Acute inflammation → CRP, Hepcidin, ferritin, fibrinogen
Negative reactants	Albumin & Transferrin levels decrease in acute inflammation

Reaction of inflammation	Principle Mediators
Vasodilation	Histamine, prostaglandins
Increased vascular permeability	Histamine, serotonin, C3a, C5a, LT C4, D4, E4
Chemotaxis, leukocyte recruitment and activation	TNF, IL-1, IL-8, chemokines, C3a, C5a, LTB4
Fever	IL-1, TNF, prostaglandins
Pain	Bradykinin , Prostaglandins, substance P
Tissue damage	ROS, lysosomal enzymes

Cytokine	Principal source	Main role in inflammation
<u>In acute inflammation</u>		
TNF	Macrophages, mast cells, T lymphocytes	Stimulates expression of adhesion molecules, secretion of cytokines, systemic effects
IL-1	Macrophages, endothelial cells	Like TNF, greater role in fever
IL-6	macrophages	Acute phase response
Chemokines	Macrophages, endothelial cells, T cells	Leukocyte recruitment and migration
IL-17	T lymphocytes	Neutrophils and monocyte recruitment
<u>In Chronic inflammation</u>		
IL-12	Dendritic cells, macrophages	Increased IF-Gamma production
IF-gamma	T lymphocytes, NK cells	Macrophage activation (classic)
IL-17	T lymphocytes	Neutrophils and monocyte recruitment

Neutrophils & Macrophages Response to Inflammation Lines of Defense

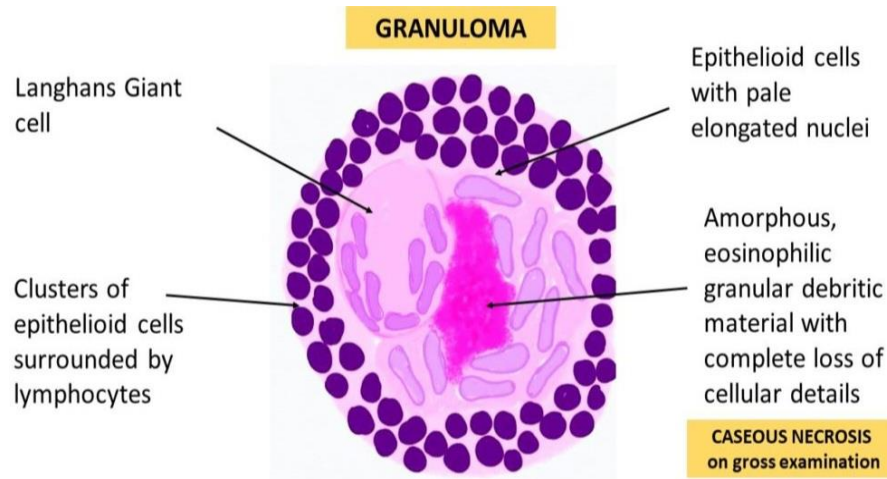
First line defence	Tissue Macrophages
Second line of defence	Neutrophils invasion of inflamed area
Third line of defence	Monocyte – Macrophage invasion of inflamed area
Fourth line of defence	Inc production of granulocytes and monocytes by bone marrow

Key Facts

- Granulocytes = Neutrophils, Basophils, Eosinophils (Remember it by NEB / BEN)
- Agranulocytes = Monocytes, Lymphocytes
- Largest cell in Blood: Monocyte
- Largest cell in bone marrow: Megakaryocytes (Platelets)
- Overall largest: Megakaryocyte > Monocyte
- Main cytokines in acute inflammation: IL-1 and TNF – Alpha
- Main cytokines in chronic inflammation: IL-12 and IFN – Gamma

Leukocyte adhesion deficiency type I (LAD I)	Defect of integrin (CD 18) leads to risk of bacterial infections, sepsis, delayed separation of umbilical cord at birth, neutrophils raised but absent at the site of infection, gingivitis. LAD III def is integrin activation defect, same features as LAD I except bleeding tendency
Leukocyte adhesion deficiency type II	Defect in selectin, recurrent infections, microcephaly, mental retardation, dwarfism and neutrophilia.
Chediak Higashi syndrome	Defect in phagolysosome formation leads to increased risk of pyogenic infections, neutropenia, giant granule formation, albinism, defective platelet plug formation
Chronic Granulomatous disease	Due to NADPH oxidase defect, impaired bactericidal effect of neutrophil MPO system, increased susceptibility of Catalase +Ve infections e.g., S Aureus, Klebsiella, candida, aspergillus

CHRONIC INFLAMMATION							
Occurs more by adaptive immunity. Over days → Lasts for weeks to months							
Causes	<ul style="list-style-type: none"> Persistent infection-e.g., viral, or parasitic infections; tuberculosis Immune mediated-e.g., autoimmune disease-self-antigens trigger inflammatory response. Persistent exposure to injurious agents – e.g., silicosis in the lung; atherosclerosis in vessels 						
Main cells	<p>Macrophages (most important cells), Lymphocytes (most abundant), Plasma cells</p> <table border="1"> <tr> <th colspan="2">Macrophage activation pathways:</th></tr> <tr> <td>Classical (M1)</td><td>It is via microbial products (endotoxins), IFN-gamma, foreign agents (crystals) Overall effect: microbicidal (by generation of ROS, lysosomal enzymes) and inflammation (by Cytokines IL1, 12, 23)</td></tr> <tr> <td>Alternate (M2)</td><td>IL 4, 13 produced by T cells activate macrophages that secrete TGF-β and IL-10 Overall effect: Anti-inflammatory, healing, tissue repair/fibrosis</td></tr> </table>	Macrophage activation pathways:		Classical (M1)	It is via microbial products (endotoxins), IFN-gamma, foreign agents (crystals) Overall effect: microbicidal (by generation of ROS, lysosomal enzymes) and inflammation (by Cytokines IL1, 12, 23)	Alternate (M2)	IL 4, 13 produced by T cells activate macrophages that secrete TGF-β and IL-10 Overall effect: Anti-inflammatory, healing , tissue repair/fibrosis
Macrophage activation pathways:							
Classical (M1)	It is via microbial products (endotoxins), IFN-gamma, foreign agents (crystals) Overall effect: microbicidal (by generation of ROS, lysosomal enzymes) and inflammation (by Cytokines IL1, 12, 23)						
Alternate (M2)	IL 4, 13 produced by T cells activate macrophages that secrete TGF-β and IL-10 Overall effect: Anti-inflammatory, healing , tissue repair/fibrosis						
Main effects or hallmarks	tissue destruction, Cellular infiltrates, Blood vessel proliferation and connective tissue deposition i.e., fibrosis and scarring of tissue						
Morphology	<ul style="list-style-type: none"> Infiltration with mononuclear cells (macrophages, lymphocytes, plasma cells) + tissue destruction + granulation tissue and fibrosis Granulomatous inflammation is distinctive pattern of chronic inflammation where the cells fail to eradicate an offending agent. Activation of T lymphocytes and macrophage activation are important events here e.g., Tuberculosis, foreign body reaction 						
Granuloma	<p>Granuloma = collection of activated epithelioid cells often surrounded by a collar of mononuclear cells (e.g., lymphocytes, plasma cells)</p> <ul style="list-style-type: none"> Epithelioid Cells are the activated macrophages – main cells of Granuloma. Giant cells are formed by Epithelioid aggregation – not necessarily present in granuloma. Types of giant cells are: Langhans cells (horseshoe shaped) in Tb, tumour cells, tumour giant cells, foreign body giant cells. Keep in mind that, the abovementioned cell type is Langhans, NOT Langerhans. <table border="1"> <tr> <th colspan="2">TYPES OF GRANULOMAS</th></tr> <tr> <td>Immune granuloma</td><td> Caused by insoluble particles typically microbes e.g., Tb, histoplasma. <ul style="list-style-type: none"> Caseating granuloma appears in T.B, histoplasmosis. Non caseating granuloma seen in Sarcoidosis, chron's disease. Stellate shaped granuloma in cat scratch disease. Actinomyces produce granuloma with abscess in jaw, head & neck region. Schistosomiasis causes granuloma formation in Urinary bladder. </td></tr> <tr> <td>Foreign body granuloma</td><td>They are non-immunogenic i.e., don't illicit any specific immune response e.g., Talc, suture and graft materials</td></tr> </table>	TYPES OF GRANULOMAS		Immune granuloma	Caused by insoluble particles typically microbes e.g., Tb, histoplasma. <ul style="list-style-type: none"> Caseating granuloma appears in T.B, histoplasmosis. Non caseating granuloma seen in Sarcoidosis, chron's disease. Stellate shaped granuloma in cat scratch disease. Actinomyces produce granuloma with abscess in jaw, head & neck region. Schistosomiasis causes granuloma formation in Urinary bladder. 	Foreign body granuloma	They are non-immunogenic i.e., don't illicit any specific immune response e.g., Talc , suture and graft materials
TYPES OF GRANULOMAS							
Immune granuloma	Caused by insoluble particles typically microbes e.g., Tb, histoplasma. <ul style="list-style-type: none"> Caseating granuloma appears in T.B, histoplasmosis. Non caseating granuloma seen in Sarcoidosis, chron's disease. Stellate shaped granuloma in cat scratch disease. Actinomyces produce granuloma with abscess in jaw, head & neck region. Schistosomiasis causes granuloma formation in Urinary bladder. 						
Foreign body granuloma	They are non-immunogenic i.e., don't illicit any specific immune response e.g., Talc , suture and graft materials						
Key Facts	<ul style="list-style-type: none"> Overall, most imp for Granuloma are: IFN – Gamma. > TNF – Alpha Most Abundant cells in Chronic inflammation are Lymphocytes. Most important cells in chronic inflammation are Macrophage. Epithelioid Cells Are Modified Macrophages. Epithelioid cells are formed by: Macrophages > Monocytes. Epithelioid cells are derived from: Monocytes. Epithelioid cells in Tb granuloma are derived from: Monocytes. Langhans type giant cells seen in T.B (NOT Langerhans). IFN-Gamma initiates Granuloma formation (most important). IL – 12 facilitates granuloma formation. TNF – Alpha maintains granuloma formation. 						



CYTOKINE	IMPORTANT ROLE
IL -1	IL1, IL6, TNF alpha → fever and sepsis, Fever → IL1 > TNF; IL 1 is osteoclast activating factor also
TNF-alpha	Fever in Pseudomonal infection; maintains granuloma and causes Cachexia in Malignancy
IL-6	stimulates acute phase reactant formation in liver
IL-2	stimulates T cells
IL-3	Stimulates Bone marrow
IL-4	Stimulate growth of B-cells and IgE production
IL-5	Stimulates IgA production & Eosinophils
IL-8	Major chemotactic for neutrophil
IL-10 & TGF-β	Anti-inflammatory cytokines
IFN-Gamma	Induction of granuloma
IL-12	Facilitates granuloma formation

REPAIR & HEALING

Repair may occur via either Regeneration or Fibrosis

Regeneration	restoration of normal structure and function of tissue.
Fibrosis	Fibrosis occurs by scar formation when normal structure and function can't be restored.
Type Of Cells According to Ability of Proliferation Or Regeneration	
Labile cells	<ul style="list-style-type: none"> Continuously dividing cells and renew themselves: e.g., skin epithelium, mucosal lining of the GIT, haematopoietic cells (blood cells). Never goes in G0 (resting phase). Chemotherapy affects these mostly. GIT Epithelium is replaced in 2 – 7 days
Quiescent cells (Stable)	<ul style="list-style-type: none"> cells divide when there is a Need e.g., hepatic, kidney, and pancreas. They go into transition from G0 → G1 phase depending Upon conditions. Liver cells regenerate in 7 – 10 days following partial hepatectomy.
Permanent cells	<ul style="list-style-type: none"> Non-dividing cells so when injured, Heal by fibrous tissue e.g., nerve cells and skeletal, Cardiac muscle cells. Always in G0 phase and don't divide. They regenerate from Stem Cells. Cells that never Reproduce: RBCs (lack Nucleus) Cells that don't regenerate: Lens > Skeletal Muscles > Nerves > Cardiac muscles. Peripheral nerves repair or regenerate at the rate of 1- 3 mm/day.

Stem cell category	Definition and Example
Totipotent	The capacity to differentiate into all possible cell types including extraembryonic tissue (Fertilized egg).
Pluripotent	The capacity to differentiate into almost all cell types except extraembryonic tissue, so they lack the ability to develop into a foetal or adult animal e.g., Embryonic stem cells
Multipotent	The potential to give rise to cells from multiple but a limited number of lineages e.g., mesenchymal stem cells
Unipotent	The capacity to differentiate into only one cell type e.g., skin
Oligopotent	The ability to differentiate into a few cell types e.g., Myeloid stem cells (they are also multipotent)

WOUND HEALING

It may occur by Primary, secondary, or Tertiary intention.

DURATION	FEATURES
Immediately after injury	Haemostasis phase: Fibrin aggregation, blood clot formation starts
Day 1	Neutrophils, blood clots,
Day 3	Neutrophils replaced by macrophages early granulation tissue release of ROS, epithelial cells migrate towards wound site, no bridging of incision gap
Day 5	Wound covered by epithelium due to maximum granulation tissue formation, collagen bridges incision gap, recovery of epidermal thickness, maximum neovascularization
Day 14	Maximum collagen deposition
Day 28	Scarring completed; wound is completely closed as fibroblasts cover the wound bed

WOUND HEALING BY INTENTION	
Primary intention	Clean wound with limited tissue loss, Wound edges easily approximated. Example: classic surgical wound closure using sutures, adhesive tapes and staples
Secondary intention	Large tissue loss, heavy contamination, wound cleaned and left opened to granulate, surgeon may pack and place drain, wound care promotes granulation
Tertiary intention	Also called delayed primary closure, often used with heavy bacterial count, wound is cleaned, debride, left opened for 4 to 5 days and then surgically closed

Factors delaying wound healing	Local factors	Oxygenation, Infection, Foreign body, Venous insufficiency
	Systemic factors	<ul style="list-style-type: none"> • Hormone: such as glucocorticoid, have anti-inflammatory effect and inhibit collagen synthesis • Vitamin C deficiency-lead to a defect in wound healing, particularly via a failure in collagen Synthesis and cross linking • Zinc deficiency: decreased fibroblast proliferation, decreased collagen synthesis, impaired wound strength and delayed epithelialization. • Stress and ischemia, Diabetes and Obesity • Alcoholism and smoking, Anaemia and malnutrition
Complications of wound healing	<ul style="list-style-type: none"> • Adhesions – abnormal attachments. Contractures may also form. • Debridement – the process of removing devitalized tissue. • Dehiscence – the breakdown of suture lines, serosanguinous discharge after 5 to 7 days. • Evisceration – the spillage of bowel from the abdominal cavity. • Fistula – pathway between two normally separate surfaces. • Gangrene- Localized death and decomposition of body tissue, resulting from either obstructed circulation or infection. 	

	<ul style="list-style-type: none"> • Granulation – new connective tissue and tiny blood vessels that Form on the surfaces of wound during the healing. • Hypertrophic Scar & Keloid (in black population) • Hematoma – A solid swelling of clotted blood within the tissues • Haemorrhage – massive blood loss (regular) blood loss comes from a paper cut
Key Facts	<ul style="list-style-type: none"> • 70% of Wound strength is achieved in 3 months, it never becomes 100% • Myofibroblast cells Mediate Wound contraction. • Remodelling of wound done by: Metalloproteinases > Collagenases > Elastases • More inflammation, granulation tissue and wound contraction mainly in secondary Healing • Most common factor or Local factor delaying wound Healing: Infection. • Most imp / common factor that delays wound healing is infection. • MC systemic factor delaying healing is Diabetes Mellitus > Anaemia > Malnutrition. • Vit C def may delay healing via dec Collagen synthesis. • Predominant Collagen in Keloid: Type 1 + Type 3 • Predominant collagen in Hypertrophic scar: Type 3 • Collagen in Early Wound Healing: Type 3, in late wound healing: Type 1
Hypertrophic scar	Develops soon after surgery, usually improves with time or appropriate surgery, itchy, painful, occurs when scar crosses skin creases and joints, no association with skin colour, more in frequency than keloids.
Keloid	Develops months after trauma, spreads outside the boundary of initial lesion, rarely improves with time, itchy, occurs on ear lobes, sternum, shoulders and rarely across joints, association with dark skin colour e.g., in black population, rare in frequency than hypertrophic scars

FACTORS	SOURCE	ROLE IN HEALING
Platelet-derived growth factor (PDGF)	Platelet, macrophages, keratinocytes	Fibroblast proliferation, chemoattraction
Vascular endothelial growth factor (VEGF)	Epidermal cell, macrophage	Angiogenesis, increase vascular permeability
Epidermal growth factor (EGF)	Platelets, macrophages, fibroblasts	Cell migration and proliferation
Fibroblasts growth factor (FGF)	Macrophages, mast cells, endothelial cells, keratinocytes, fibroblasts	Angiogenesis, fibroblast proliferation, keratinocyte migration
Transforming growth factor B-1 (TGF-B)	Platelets, macrophages, keratinocytes, fibroblasts, lymphocytes	ECM synthesis, granulation tissue formation, re-epithelization
TNF	Neutrophil, macrophages	Growth factor expression, re-epithelization
IL-1	Neutrophil, macrophages, fibroblast	Inflammation, re-epithelization
IL-6	Neutrophil, macrophages, fibroblast	re-epithelization, granulation
IL-8	Neutrophil, macrophages	re-epithelization

TYPE OF WOUND BASED ON BACTERIAL LOAD	
Clean	<ul style="list-style-type: none"> Elective surgical wound where GI, GU or biliary tract is not opened. risk of sepsis: 1.8 - 2.6% No inflammation, pus, or faecal matter Examples: thyroid, parotid surgery, knee replacement, uncomplicated hernia repair
Clean-contaminated	<ul style="list-style-type: none"> Elective surgical wound where GI, GU or biliary tract is opened without spillage of contents, risk of sepsis (4.8 – 6.7%), No inflammation, pus, or faecal matter Examples: elective/interval cholecystectomy, appendectomy, resection of a part of gut, renal stone without UTI
Contaminated	<ul style="list-style-type: none"> Elective surgical wound where GI, GU or biliary tract is opened with gross spillage of contents, risk of sepsis (5.6 – 8.6 %), inflammation +Ve, no pus or faecal matter Traumatic wound – early intervention (< 6 hours) Examples: Emergency cholecystectomy/appendectomy, duodenal or intestinal perforation, RTA laceration
Dirty	<ul style="list-style-type: none"> Traumatic wound – delayed intervention (> 6 hrs), purulent substance contained in wound +Ve inflammation, pus +, faecal matter +, risk of sepsis = 8.5 – 11.4% Examples: Peritonitis, abscess, resection of infarcted bowel, necrotizing fasciitis, Fournier's gangrene, open fracture repair, RTA laceration

Systemic inflammatory response syndrome (SIRS)	<p>Two or more of the:</p> <ul style="list-style-type: none"> Temperature > 38 C or < 36 C Tachycardia > 90bpm Respiratory rate > 20 bpm or PaCo₂ < 4.3 Kpa WBC count > 12 × 10⁹/L or < 4 × 10⁹/L (OR) > 10% immature band cells
Sepsis	<ul style="list-style-type: none"> SIRS due to severe infection, +Ve evidence of bacterial in blood stream confirmed by cultures. Culture +Ve (e.g., blood culture) is mandatory for diagnosis of sepsis
Bacteraemia	<ul style="list-style-type: none"> Presence of bacteria in blood stream <u>±</u> SIRS
Sepsis induced hypotension	<ul style="list-style-type: none"> Systolic BP > 90 mmHg or reduction of > 40 mmHg from baseline in the absence of other causes of hypotension may be responsive to resuscitation
Septic shock	<ul style="list-style-type: none"> Sepsis induced hypotension despite adequate fluid or vasopressin resuscitation along with perfusion abnormalities that may include but are not limited to: Lactic acidosis, oliguria, altered mental status
Multiple organ dysfunction syndrome (MODS)	<ul style="list-style-type: none"> Dysfunction of liver, kidney, heart, lungs, GIT caused by severe hypoperfusion and other complication of SIRS, including physiological derangements in which organ function is not capable of maintaining homeostasis

Feature	Ulcer Type			
	Venous	Arterial	Neuropathic Diabetic	Pressure
Underlying condition	Varicose veins, previous deep-vein thrombosis, obesity, pregnancy, recurrent phlebitis	Diabetes, hypertension, smoking, previous vascular disease	Diabetes, trauma, prolonged pressure	Limited mobility
Ulcer location	Area between the lower calf and the medial malleolus	Pressure points, toes and feet, lateral malleolus and tibial areas	Plantar aspect of foot, tip of the toe, lateral to fifth metatarsal	Bony prominences, heel
Ulcer characteristic	Shallow and flat margins, moderate-to-heavy exudate, slough at base with granulation tissue	Punched out and deep, irregular shape, unhealthy wound bed, presence of necrotic tissue, minimal exudate unless infected	Deep, surrounded by callosus, insensate	Deep, often macerated
				
Condition of leg or foot	Hemosiderin staining, thickening and fibrosis, eczematous and itchy skin, limb edema, normal capillary refill	Thin shiny skin, reduced hair growth, cool skin, pallor on leg elevation, absent or weak pulses, delayed capillary refill, gangrene	Dry, cracked, insensate, calluses	Atrophic skin, loss of muscle mass
Treatment	Compression therapy, leg elevation, surgical management	Revascularization, anti-platelet medications, management of risk factors	Off-loading of pressure, topical growth factors	Off-loading of pressure; reduction of excessive moisture, shear, and friction; adequate nutrition

PAST PAPERS BCQs

1. Neutrophils can't attach endothelium due to deficiency of: LFA – 1 or CD 18 (integrin)
2. WBCs attach to endothelium via ICAM – 1
3. Phagocytosis is done by: Neutrophils (if not mentioned in Blood or tissues, prefer Neutrophils)
4. Hot water spilled onto finger leads to development of Bulla, later fever & Erythema → Serous inflammation
5. Foam cells on atheroma formed by: Macrophages
6. Purulent (suppurative) inflammation --- localized proliferation of pus-forming organisms, such as S. Aureus (e.g., skin Abscesses), acute appendicitis, cellulitis & furunculosis etc.
7. Fibrinous inflammation is due to increased vessel permeability, with deposition of Fibrin-rich exudate on the surface of the tissue. Commonly occurs on the serosal lining of the pericardium, peritoneum, or pleura.
8. Serous inflammation is an inflammation with a thin, watery exudate that has an insufficient amount of Fibrinogen to produce fibrin. Examples—blister in second degree burns or Sun burn & viral pleuritis.
9. Keloids extend beyond wound margins, more in black population, contain Type 1 & Type 3 collagen
10. Hypertrophic scar is in wound margins, abundant type 3 collagen, may develop in 4 weeks by thermal injury or trauma.
11. For abscess, Ulceration & wound contamination: secondary intention healing is best
12. Max wound strength reached in 3 months – 70 %
13. Remodelling of tissues done by: Metalloproteinases (requires Zinc) > Collagenases > Elastases
14. Pain mediated by: Bradykinin
15. Healing of wound done by: Microfilaments (Actin)
16. Lymphocytes, fibroblasts, macrophages & Epithelioid cells seen in: Granulomatous inflammation
17. Immediate (first / earliest) event in Acute Inflammation: Vasoconstriction
18. Initial mediator of inflammation is Histamine
19. Albumin & Transferrin levels don't raise in acute inflammation
20. ESR is directly proportional to Fibrinogen & inversely to Albumin
21. High ESR → due to LOW ALBUMIN > INC Fibrinogen levels
22. ESR > 100 in Multiple myeloma
23. The Main difference between primary and 2ndry intention is Wound Contraction
24. CRP is important Marker or IHD
25. Margination – Rolling – Adhesion – Transmigration – chemotaxis (remember this sequence as it is)
26. Post op infection delays healing due to Collagen destruction
27. Enhanced phagocytic activity for better killing via Opsonization process
28. After Tissue injury, haemostasis / Blood clotting occurs by Contact of Blood with Collagen
29. Protein deficiency is least imp in wound healing. UV light is also the least imp factor in delaying healing
30. Fibroblasts release: Amorphous Substance. Fibrocartilage contains: Abundant collagen
31. Part of innate immunity active against Covid – 19, viruses / Tumour cells: NK cells
32. Vasodilation by: PGE 2, PGF 2 alpha & PG- I (Prostacyclin's)
33. Vasoconstriction via: Thromboxane A2, LTD4, LTE4, LTC4
34. Opsonization by: C3b
35. Repair of inflammation begins by 24 hrs. Maximum chemotaxis occurs in acute inflammation
36. Lymphatics Return tissue fluid & Resolve inflammation.
37. Epithelioid Cells: Are modified Macrophages (activated by INF – Gamma released from CD4+ Cells)
38. Epithelioid cells are **formed** by: Macrophages > Monocytes
39. Epithelioid cells are **derived** from: Monocytes. Epithelioid cells in Tb granuloma are derived from: Monocytes
40. For Sarcoidosis: Non Caseating granuloma > Granuloma with Asteroid bodies
41. Soft Granuloma: Tb; Hard granuloma: Sarcoidosis
42. For Granuloma diagnosis: Epithelioid cells are hallmark /important
43. Cat scratch disease: Stellate or round granuloma
44. Pus contains dead neutrophils. Most abundant cells in Chronic inflammation: Lymphocytes
45. Inadequate granulation Tissue or deficient scar may lead to: Wound Dehiscence
46. Type of inflammation in carbuncle = Purulent (acute inflammation)
47. Decrease Cross linking in Collagen: Cu deficiency
48. Fibronectin is the key adhesion glycoprotein in Granulations tissue formation
49. Vit C def leads to: decrease Collagen formation > defective collagen
50. Skin appendages play role in healing after burn

51. IL – 10 & TGF – Beta: anti-inflammatory (play role in healing)
52. LANGHAN's type giant cell seen in Tb granuloma
53. Granulation tissue is hallmark of Repair
54. Granulation Tissue = activated Fibroblasts, Macrophages, Lymphocytes, blood vessels
55. Vasculo-genesis refers to the development of new vessels from primordial endothelial stem cells, whereas angiogenesis denotes the formation of vessels from pre-existing capillary structures.
56. VEGF plays key role in angiogenesis & Healing
57. Immediate mediator of inflammation: histamine. Delayed mediator of inflammation: leukotrienes & Prostaglandins
58. Fever mediators: IL-1 > TNF alpha
59. Important Role of Bradykinin: increase vascular permeability
60. Phagocytosis factor: C3b. Potent chemotactic factor: c5a > LTB4
61. T cell activator: IL 1. Pain Mediator: Bradykinin > Prostaglandins E1 (PGE)
62. IL – 1 mediates fever via action of Prostaglandins
63. Secreted by endothelium = prostacyclin
64. Rolling of neutrophils: selectins. Neutrophil adhesions: integrins
65. Mast cells release: Histamine. Platelets are rich source of: Serotonin
66. Helper cells are CD4+; Cytotoxic cell are CD8+
67. Natural killer cells: cell of innate immunity, Anti-tumour cell & kills virus infected cells
68. Fluid in serous cavity is called effusion
69. Transmigration occurs via PECAM / CD – 31. Most bactericidal action is of HOCL
70. LAD 1 def is INTEGRIN defect – in which delayed separation of umbilical cord & absent neutrophils at infection site
71. PDGF is most potent inflammatory mediator, it is produced by Macrophages & Platelets
72. Basic FGF secreted by Macrophages whereas Acidic FGF secreted by: Neural tissues
73. Macrophages are major scavengers
74. 1 st line phagocyte in tissue: Macrophages; in Blood: neutrophils
75. 1 st line of defence on surfaces and overall 1 st line: Skin
76. Fibrinopeptide increase Vascular permeability
77. Neuropeptide increase Neurogenic inflammation
78. Angiogenesis is the role of: Basic FGF, VEGF & PDGF. (VEGF – Key role)
79. In healing by primary intention: Sutures are used, no wound contraction, no role of Myofibroblasts
80. Cells of GIT, Urinary tract & Hematopoietic tissues are Labile cells
81. Can't regenerate: Lens > Skeletal muscle > Neuron > cardiac muscles
82. TGF – B plays imp role in Healing process & fibrosis
83. Basophile are seen in Blood whereas Mast cells present in Tissue
84. IFN – Gamma is most imp for granuloma formation
85. Inc Vascular permeability leads to exudate formation in inflammation
86. In sarcoidosis granuloma: T cells are increased
87. Neutrophils are seen in 24 hrs after infection
88. In appendicitis: fever is caused by cytokines (IL – 1)
89. Low cell count & Low proteins present in Transudate
90. In abscess enzymes are released by Neutrophils
91. Infection is most common Local factor delaying Healing
92. DM > Anaemia is the most common systemic factor delaying Healing.
93. For Sepsis: Blood Culture must be positive.
94. 70% of Wound strength is achieved in 3 months, it never become 100%
95. Myofibroblast cells Mediate Wound contraction
96. IL4 \rightarrow stimulates IgE production. IL5 \rightarrow stimulates IgA production & Eosinophils also.
97. Liver cells regenerate in 7 – 10 days following partial hepatectomy
98. Largest cell in Blood: Monocyte
99. Largest cell in bone marrow: Megakaryocytes (Platelets)
100. Overall largest: Megakaryocyte > Monocyte
101. Main cytokines in acute inflammation: IL-1 & TNF – Alpha
102. Main cytokines in chronic inflammation: IL-12 & IFN – Gamma
103. Dense granules + Ig E. = Basophils

104. IgE is present on Both Basophils + Mast cells
105. Venous Ulcers most commonly on Gaiter's area i.e., Medial Malleolus
106. Edges of Tb Ulcer are: UNDER MINED
107. Trophic (Diabetic) ulcer: Punched out margins – also in Syphilis, Pressure ulcers (Bed sores)
108. Healing Ulcer has Sloping edges
109. Squamous cell Carcinoma: Everted margins / edges – Malignant ulcer.
110. Basal cell carcinoma: Rolled – out margins (Rodent ulcer)
111. Interval Cholecystectomy is a type of Clean – Contaminated wound (type II Wound)
112. Wound is cleaned, debrided and left opened for some days – later closed: Type of Healing is Tertiary intention
113. Most common site of pressure sore seen on – Ischium
114. Most common site of Keloid – Sternum
115. Negativity of basement membrane is due to: Heparin sulphate > Laminin
116. Laminin is the most abundant glycoprotein in basement membrane
117. PDGF stimulates fibroblast growth for collagen synthesis
118. EGF stimulates cell growth via tyrosine kinases
119. Inflammatory phase of healing: up to 3 days after wound, macrophages present 02 days later
120. Delayed Proliferative phase of healing or 2 nd phase in: Vit C & Cu deficiency
121. Collagenases require Zn break type III collagen in remodelling phase.
122. For Fibrosis: TGF – Beta > FGF
123. Only anaemia with decrease ESR: Sickle cell anaemia
124. ESR increases in: Anaemias, infection, inflammation, malignancy, ESRD & Pregnancy, Hypoalbuminemia
125. ESR decreases in: Polycythaemia, sickle cell anaemia, Low fibrinogen
126. Persistent acute inflammation by: IL – 8
127. Pro- calcitonin raises in Bacterial infection
128. Iron haemostasis is via Ferritin. Iron haemostasis maintained by: HEPCIDIN
129. Iron haemostasis controlled by: Hepcidin > Transferrin
130. Keloids present on: Earlobes, Face, Upper Limbs whereas Hypertrophic scars on: Sternum or chest
131. Keloids recur frequently than HS
132. Cell to cell connection (also during embryonic development): cadherin
133. Cell to ECM connection via integrins.
134. ICM to ECM connection via intermediate filaments

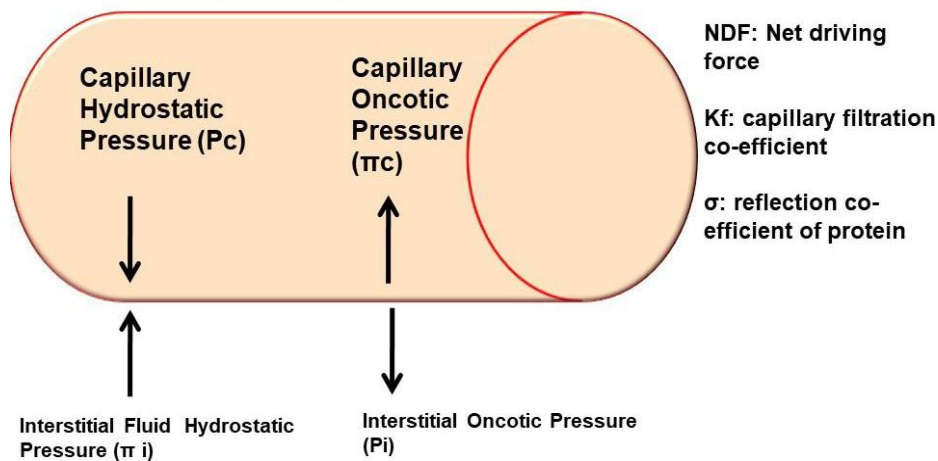
HEMODYNAMIC DISORDERS & SHOCK

EDEMA	<ul style="list-style-type: none"> Accumulation of excessive fluid in interstitial compartment (ECF) causing swelling is called edema. It becomes evident when fluid exceeds 2.5 – 3L in interstitial 																								
Types of Edema	<p>Two Clinical types as follows:</p> <ol style="list-style-type: none"> Pitting edema: in Congestive Heart failure, Renal failure, Liver cirrhosis, Chronic venous insufficiency, and Pregnancy Non – Pitting edema: Lymphedema and Myxoedema <p>Other Types:</p> <ul style="list-style-type: none"> Generalized Edema or Anasarca is due to systemic causes e.g., CHF, RF, Cirrhosis of Liver. Usually, the result of raised intravascular Volume. Localized Edema is seen in allergy, cellulitis, DVT, lymphedema, chronic venous insufficiency. Organ specific edema: cerebral edema, Pulmonary edema etc. 																								
Pathophysiology Of edema	<p>STARLING FORCES</p> <p>There are 4 Starling forces acting on the fluid moving across capillary:</p> <p>Two hydrostatic pressures:</p> <ol style="list-style-type: none"> Capillary hydrostatic pressure (Pc) – pushes fluid out of vessel. Interstitial fluid hydrostatic pressure – tends to push fluid inside vessel. <p>Two osmotic pressures:</p> <ol style="list-style-type: none"> Interstitial fluid colloid osmotic pressure – outward force (pushes fluid outside vessel wall) Plasma Colloid osmotic pressure – inward force (pulls fluid inside vessel wall) <table border="1"> <thead> <tr> <th colspan="2">Mean forces tending to move fluid outward</th></tr> </thead> <tbody> <tr> <td>Mean capillary pressure</td><td>17.3 mmHg</td></tr> <tr> <td>Negative interstitial fluid pressure</td><td>3.0 mmHg</td></tr> <tr> <td>Interstitial fluid colloid osmotic pressure</td><td>8.0 mmHg</td></tr> <tr> <td>Total Outward force</td><td>28.3 mmHg</td></tr> </tbody> </table> <table border="1"> <thead> <tr> <th colspan="2">Mean force tending to move fluid inward</th></tr> </thead> <tbody> <tr> <td>Plasma colloid osmotic pressure</td><td>28.0 mmHg</td></tr> <tr> <td>Total inward force</td><td>28.0 mmHg</td></tr> </tbody> </table> <table border="1"> <thead> <tr> <th colspan="2">Summation of mean forces</th></tr> </thead> <tbody> <tr> <td>Outward</td><td>28.3 mmHg</td></tr> <tr> <td>Inward</td><td>28.0</td></tr> <tr> <td>Net outward force</td><td>0.3 mmHg</td></tr> </tbody> </table> <p>The above-mentioned values may vary, but the concept of Starling inward/outward forces is the same</p> <ul style="list-style-type: none"> At Arteriolar end: Hydrostatic pressure > Oncotic pressure → Fluid passes into Interstitium. At Venule end: Oncotic pressure > Hydrostatic pressure → Fluid returns capillary bed. Arteriolar constriction is a protective factor against edema. 	Mean forces tending to move fluid outward		Mean capillary pressure	17.3 mmHg	Negative interstitial fluid pressure	3.0 mmHg	Interstitial fluid colloid osmotic pressure	8.0 mmHg	Total Outward force	28.3 mmHg	Mean force tending to move fluid inward		Plasma colloid osmotic pressure	28.0 mmHg	Total inward force	28.0 mmHg	Summation of mean forces		Outward	28.3 mmHg	Inward	28.0	Net outward force	0.3 mmHg
Mean forces tending to move fluid outward																									
Mean capillary pressure	17.3 mmHg																								
Negative interstitial fluid pressure	3.0 mmHg																								
Interstitial fluid colloid osmotic pressure	8.0 mmHg																								
Total Outward force	28.3 mmHg																								
Mean force tending to move fluid inward																									
Plasma colloid osmotic pressure	28.0 mmHg																								
Total inward force	28.0 mmHg																								
Summation of mean forces																									
Outward	28.3 mmHg																								
Inward	28.0																								
Net outward force	0.3 mmHg																								
Causes and Mechanism	<table border="1"> <thead> <tr> <th>Mechanism</th><th>Causes</th></tr> </thead> <tbody> <tr> <td>↑ Hydrostatic pressure</td><td> <ul style="list-style-type: none"> Venous obstruction/insufficiency: Heart failure, cirrhosis, DVT, pulmonary HTN Volume expansion: Heart failure, renal failure, pregnancy, NSAIDs, salt overload Arteriolar vasodilation: Ca channel blockers e.g., Nifedipine, amlodipine </td></tr> <tr> <td>↓ Oncotic pressure</td><td>Hypoalbuminemia: Liver cirrhosis, nephrotic syndrome, malnutrition</td></tr> <tr> <td>↑ Capillary permeability</td><td>Sepsis, cellulitis</td></tr> <tr> <td>Lymphatic obstruction</td><td> Infections: or infestations e.g., Filariasis (Wuchereria bancrofti, Brugia malayi) Tumours: lymph node dissection, infiltration of lymphatics </td></tr> <tr> <td>Miscellaneous</td><td>Hypothyroidism</td></tr> </tbody> </table>	Mechanism	Causes	↑ Hydrostatic pressure	<ul style="list-style-type: none"> Venous obstruction/insufficiency: Heart failure, cirrhosis, DVT, pulmonary HTN Volume expansion: Heart failure, renal failure, pregnancy, NSAIDs, salt overload Arteriolar vasodilation: Ca channel blockers e.g., Nifedipine, amlodipine 	↓ Oncotic pressure	Hypoalbuminemia: Liver cirrhosis, nephrotic syndrome, malnutrition	↑ Capillary permeability	Sepsis, cellulitis	Lymphatic obstruction	Infections: or infestations e.g., Filariasis (Wuchereria bancrofti, Brugia malayi) Tumours: lymph node dissection, infiltration of lymphatics	Miscellaneous	Hypothyroidism												
Mechanism	Causes																								
↑ Hydrostatic pressure	<ul style="list-style-type: none"> Venous obstruction/insufficiency: Heart failure, cirrhosis, DVT, pulmonary HTN Volume expansion: Heart failure, renal failure, pregnancy, NSAIDs, salt overload Arteriolar vasodilation: Ca channel blockers e.g., Nifedipine, amlodipine 																								
↓ Oncotic pressure	Hypoalbuminemia: Liver cirrhosis, nephrotic syndrome, malnutrition																								
↑ Capillary permeability	Sepsis, cellulitis																								
Lymphatic obstruction	Infections: or infestations e.g., Filariasis (Wuchereria bancrofti, Brugia malayi) Tumours: lymph node dissection, infiltration of lymphatics																								
Miscellaneous	Hypothyroidism																								
Key Facts	<ul style="list-style-type: none"> Edema in Heart failure is due to increase Hydrostatic Pressure Edema worsens in CHF is due to Salt and Water Retention Edema in Hypertension is due to increase Hydrostatic Pressure 																								

- Edema in Nephrotic syndrome or Liver Cirrhosis: Hypoalbuminemia → dec Plasma Oncotic Pressure
- Edema in Nephritic syndrome: Salt & Water retention
- In inflammation, edema due to increases Vascular permeability.
- Cause of Lymphatic obstruction: Infection and Neoplasia commonly
- Parasites live in: Lymphatic system mostly.
- Oncotic pressure is the Osmotic pressure of: Proteins.
- Peri- orbital edema seen in: Renal failure / Nephrotic syndrome.
- Most common causes of generalized peripheral edema: CHF, Nephrotic syndrome, Liver Cirrhosis

Starling Forces across capillary wall

$$NDF = K_f (P_c - P_i) - \sigma (\pi_c - \pi_i)$$



LIGHT'S CRITERIA

TRANSUDATE	EXUDATE
Specific gravity < 1.012	Specific gravity > 1.012
Low cell count	High cell count
Low protein: $\leq 3\text{gm} / \text{dl}$ ($30\text{g} / \text{L}$)	High protein > $3\text{gm}/\text{dl}$
Formed due to increase Hydrostatic pressure	Formed by increase Vascular Permeability
Examples: CHF, Nephrotic syndrome & Liver Cirrhosis	E.g., Inflammation, Malignancy, Tb, Peritonitis

THROMBOSIS

Formation of blood clot within blood vessel or circulation. It is an abnormal condition.

Pathogenesis (Virchow's triad)	Virchow's Triad: It explains the pathogenesis of thrombus formation. <ol style="list-style-type: none"> Endothelial injury – most imp factor Stasis – an imp independent factor (Prolonged bed rest or Immobilization) Hypercoagulability states (primary and secondary causes) <p>Primary causes → Genetic factors (Factor V Laden Mutation & Prothrombin gene mutation)</p> <p>Secondary causes → Antiphospholipid antibody syndrome, Trauma, Burn, OCPs, surgery.</p> 				
Morphology	<ul style="list-style-type: none"> Thrombi can have grossly (and microscopically) apparent laminations called lines of Zahn, these Represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers. Such lines are significant only in that they represent thrombosis in the setting of flowing blood; their Presence can therefore potentially distinguish antemortem thrombosis from the bland Non laminated clots that occur in the postmortem state. Most venous thrombi occur in the superficial or deep veins of the leg. Superficial venous thrombosis. In the saphenous system, particularly Usually occur when there are varicosities. Deep thrombi in the larger leg veins at or above the knee joint (e-&. Popliteal, femoral, and iliac Veins) are more serious because they may embolize. Cardiac failure is an obvious reason for stasis. Lines Of Zahn seen in Coralline Thrombus > Ante-mortem thrombus > Recent Thrombus Chicken-Fat Appearance: Seen in Postmortem clot. Dark red homogenous, not adherent to vessel wall. <table border="1"> <thead> <tr> <th>Antemortem Thrombi</th><th>Postmortem Clot</th></tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> Dry granular, firm & friable Laminated red & white areas. Adherent to vessel wall Lines of Zahn present </td><td> <ul style="list-style-type: none"> Gelatinous, soft & rubbery Dark Red appearance Non – adherent to vessel wall or endocardium Chicken fat appearance, no lines of Zahn seen </td></tr> </tbody> </table>	Antemortem Thrombi	Postmortem Clot	<ul style="list-style-type: none"> Dry granular, firm & friable Laminated red & white areas. Adherent to vessel wall Lines of Zahn present 	<ul style="list-style-type: none"> Gelatinous, soft & rubbery Dark Red appearance Non – adherent to vessel wall or endocardium Chicken fat appearance, no lines of Zahn seen
Antemortem Thrombi	Postmortem Clot				
<ul style="list-style-type: none"> Dry granular, firm & friable Laminated red & white areas. Adherent to vessel wall Lines of Zahn present 	<ul style="list-style-type: none"> Gelatinous, soft & rubbery Dark Red appearance Non – adherent to vessel wall or endocardium Chicken fat appearance, no lines of Zahn seen 				
Fates of Thrombus	Dissolution, Organization and Recanalization, Emboli formation, Propagation, Abscess formation.				

EMBOLISM

A detached intravascular solid, liquid, or gaseous mass that is carried by blood to a site distant from its origin.
 99% of cases are due to dislodged thrombus.

Types	<ol style="list-style-type: none"> Based on Location of Blockade: Pulmonary/venous embolism, Brain embolism & arterial embolism (post MI) Based on Blockade Material: Thromboembolism, Air embolism, Fat embolism, Amniotic fluid embolism & Septic Bases on Consistency: Solid, Liquid, Air or Gas Emboli. Paradoxical Emboli: A Venous embolus that becomes Arterial due to ASD / VSD Saddle Emboli: A type of Venous emboli that lodges in the Main Pulmonary artery or Bifurcation of Pulmonary artery or branches
Pulmonary embolism	<ul style="list-style-type: none"> Commonly arises from Deep veins of leg (Femoral or Popliteal vein) At first, it goes into IVC and Right Heart and finally it Lodges into the Branches of Pulmonary artery or Lungs. Large sized embolus causes death due to Acute RHF.
Fat/marrow embolism	<ul style="list-style-type: none"> History of Long bone fracture or soft tissue trauma. Presents 1—3 days later after injury with: Dyspnoea, neurological symptoms, anaemia, low Platelets. Fatal in 10% cases
Air/Gas embolism	<ul style="list-style-type: none"> History of obstetric procedures, consequence of chest wall injury or While passing CVP air embolism can develop. > 100 ml of air is required to produce a clinical effect. Caisson's disease is an example of gas embolism

Amniotic fluid embolism	<ul style="list-style-type: none"> ○ A complication of labour and immediate postpartum period (1 in 50,000 deliveries). ○ Most lethal type of embolism with the mortality rate 20%- 40%. ○ Presents with sudden severe dyspnoea, cyanosis, and hypotensive shock, followed by coma and death
Systemic embolism	<ul style="list-style-type: none"> ○ Arterial emboli in systemic circulation Mostly arises from intracardiac mural thrombi (Left Ventricular thrombus) in 80% cases or mitral Valve disease. ○ The major sites of embolization are Lower extremities- 70% and Brain – 10 %.

Decompression Sickness & Caisson's Disease

- A form of gas embolism common in deep sea divers due to Nitrogen gas – forced out of alveoli and dissolved in blood and tissue.
- **Caisson's disease:** caused by persistence of gas emboli in bone, producing aseptic necrosis (bone Infarction)
- Treated with Hyperbaric oxygen – Hyperbaric O₂ is also use for Tx of gas gangrenes and CO poisoning also.
- Prefer decompression sickness for usage of HBO₂ therapy.
- **Complication of hyperbaric O₂:** Pneumothorax, myopia, middle ear Barotrauma and oxygen Induced seizure.

THROMBOGENESIS

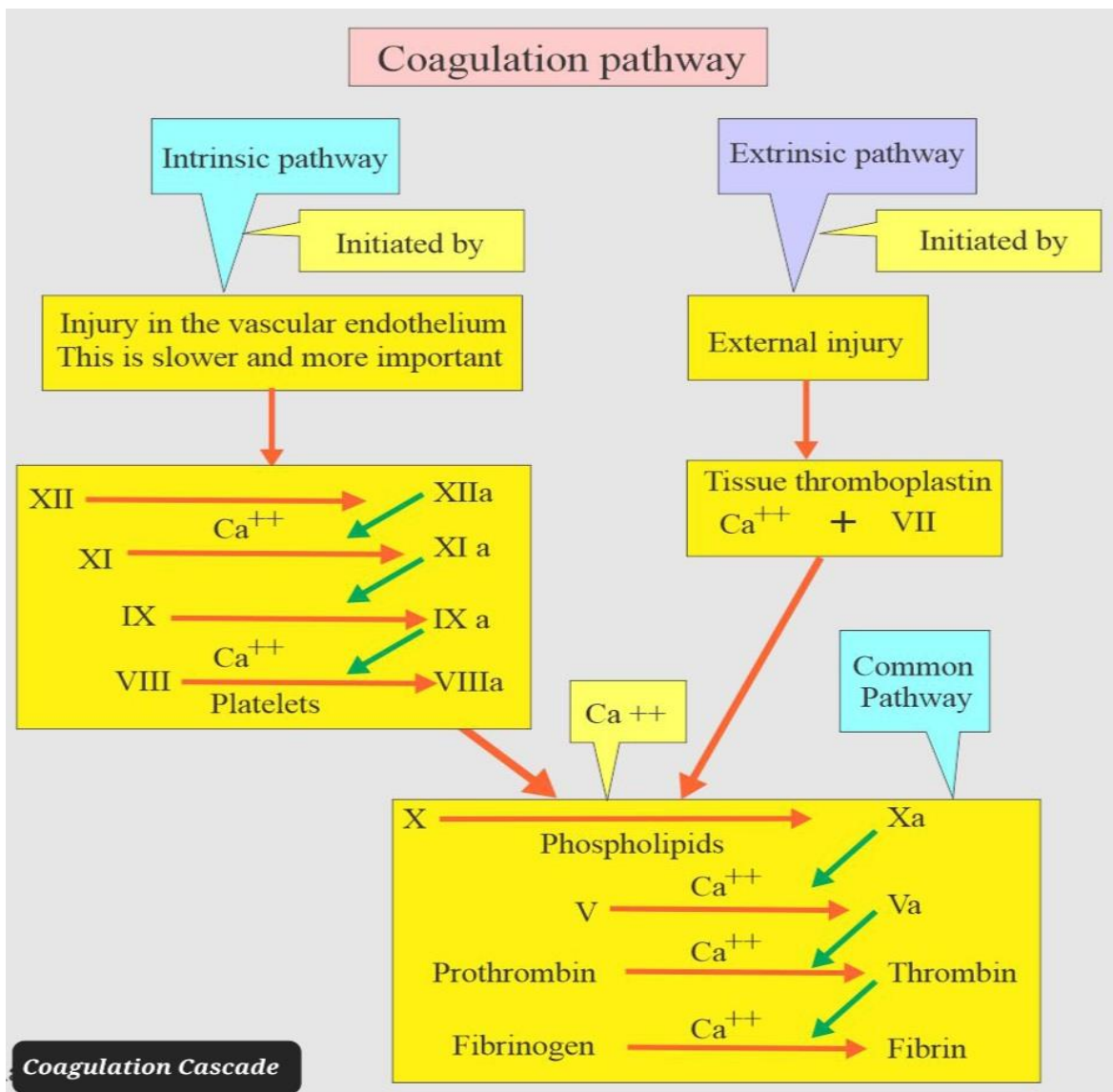
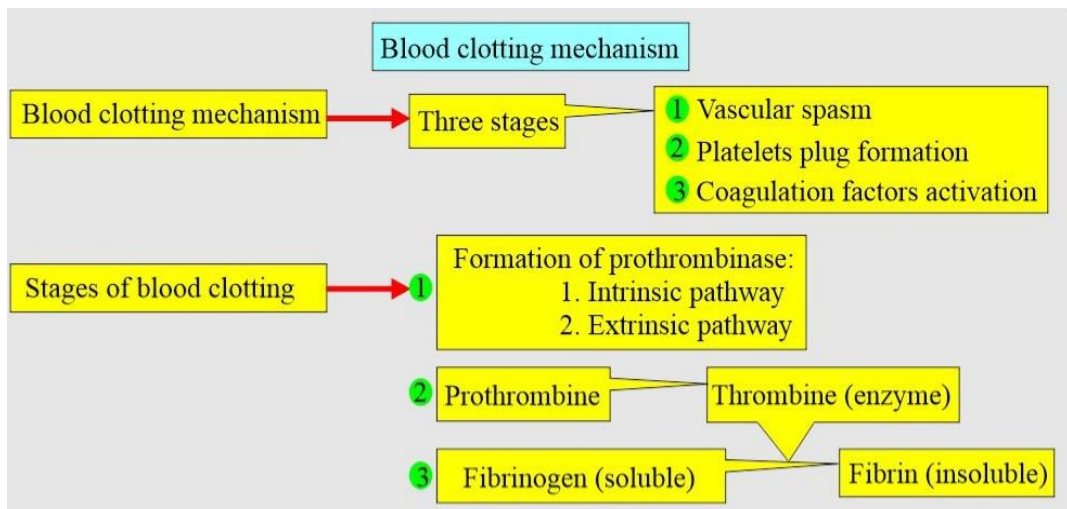
It results from interaction of Platelets, damaged endothelium, and Coagulation cascade.

Platelets	<ul style="list-style-type: none"> ○ Platelet adhesion → Vessel's injury → endothelial exposure → platelets adhere to it and release ADP, histamine, and serotonin → activation of coagulation cascade. ○ Platelets adhere to rough endothelial surface. ○ Upon activation platelets change shape from Flat to Spherical (round) ○ Platelet aggregation: Platelets stick to each other helped by TxA₂ and PAF ○ Platelet plug is stabilized by fibrinogen
Endothelial cells	<ul style="list-style-type: none"> ○ Intact endothelial cells oppose coagulation by synthesizing and releasing PGI₂ and NO (which Inhibits platelet aggregation) also by taking up, inactivating and clearing thrombin.
Coagulation cascade	Extrinsic pathway Mechanism <ul style="list-style-type: none"> • Initiated by tissue factor, which activates factor VII and forms a tissue factor-factor VII-a complex, The complex initiates coagulation through the activation of factor X to factor Xa (and Additionally factor IX to factor IX-A). • Factor Xa converts prothrombin (factor I) to thrombin (factor IIa). • Factor Va is a cofactor required in the conversion of prothrombin to thrombin. • Thrombin converts fibrinogen to fibrin. • The prothrombin-mediated cleavage of fibrinogen results in a fibrin monomer, which is polymerized and stabilized by factor XIII, thus forming the fibrin clot.
	Intrinsic pathway Mechanism <ul style="list-style-type: none"> • Involves the activation of all clotting factors except for factors VII and XIII, when factor XII comes in contact with collagen, it is converted into activated factor XIIa, which in turn converts factor XI to activated XI-A • Activated factor IX activates factor Xa in presence of calcium and factor VII
	Common pathway <ul style="list-style-type: none"> • Factor Xa converts prothrombin into thrombin which forms the fibrin clot. • Factor 13 helps in cross linking of that fibrin clot and stabilizes it also. • Common factors are factor 1,2,5,10, $5 \times 2 = 10 \times 1$

Clotting Factor No.	Name of Factor	Extrinsic Pathway	Intrinsic Pathway
1.	Fibrinogen	It is activated by tissue Thromboplastin (Factor III) Prothrombin Time is used to check extrinsic pathway which measures factors: 2, 5, 7, 9, 10	It is activated by Subendothelial collagen. aPTT is used to check this pathway. Which measures factors: 1, 2, 5, 8, 9, 10, 11, 12; Except 7, 13
2.	Prothrombin	Warfarin acts on Extrinsic pathway. Given Orally. Inhibits Vit K epoxide reductase and blocks Gamma carboxylation of vit K dependant factors: 2,7,9,10	Heparin acts on intrinsic pathway. It is given IV in DVT in pregnancy and Subcutaneous route is the routinely used route. Heparin activates anti thrombin 3 and inhibits factor 2 + factor 10.
3.	Tissue Factor or Tissue thromboplastin		
4.	Calcium		
5.	Labile factor	Remember the Extrinsic pathway by: PET – 7: Prothrombin time, Extrinsic, factor 7 All factors except 7 & 13 are included in intrinsic pathway. ■ Intrinsic pathway depends upon: Vessel injury, Collagen contact, factors 12, 11, 9, 8 and Calcium (4) ■ Extrinsic factor depends upon: Tissue factor or Tissue thromboplastin, factor 7, vessel injury and calcium. Normal PT value: 10 – 14 seconds; aPTT normal: 25 – 35 seconds	
6.	No factor (N/A)		
7.	Stable factor		
8.	Antihemophilic factor A		
9.	Christmas factor or Anti homophilic factor B		
10.	Stuart power factor		
11.	Plasma Thromboplastin antecedent		
12.	Hageman factor		
13.	Fibrin-Stabilizing factor		

Key Facts

- Tissue factor / Factor III plays main role in DIC – most common coagulopathy in Trauma.
- Factor 10 = Stuart power factor & Factor 7 = Stable factor
- Factor 12 = Hageman factor – activates Pre – kallikrein to Kallikrein which converts High Molecular weight Kininogen to Bradykinin. Kallikrein also activates Plasminogen → Plasmin.
- Platelets function by: ADP & Thromboxane A2. Platelets change shape from flat to Spherical when activated.
- Aspirin partially inhibits thromboxane A2 (TXA2)



SHOCK	
A state of systemic hypoperfusion due to decreased effective circulating blood volume leading to impaired cellular respiration due to underlying Tissue hypoxia.	
Pathophysiology	<p>Circulatory failure resulting in inadequate perfusion of organs. Not meeting the needs of organs.</p> <p>Shock can result from:</p> <ul style="list-style-type: none"> • <u>Inadequate Cardiac Output:</u> Hypovolemia: Resulting from bleeding, trauma, bleeding from surgery, burns, severe vomiting/diarrhoea, heat exhaustion. Pump Failure: Cardiogenic shock resulting from ACS, Arrhythmias, Aortic Dissection, PE, Tension Pneumothorax, Cardiac Tamponade. • <u>Peripheral Circulatory Failure</u> (Loss of systemic vascular resistance) Sepsis, Anaphylaxis, Neurogenic, Endocrinological and Drugs Induced. • <u>Features Common to All Types of Shock</u> <ul style="list-style-type: none"> • SBP < 90mmHg & MAP < 65mmHg • Oliguria i.e., urine output less than 500ml/day. • Tachycardia (Except Neurogenic shock) • Increased capillary refill time • Decreased CVP (Except Cardiogenic shock) • Cold clammy peripheries (Except Septic shock, warm moist here)
TYPES OF SHOCK	
Hypovolemic, Cardiogenic, Obstructive, Distributive (Anaphylactic, Spinal or Neurogenic & Septic shock)	
Hypovolemic shock	<ul style="list-style-type: none"> • Same features of shock and Easiest to diagnose. • Results from Blood loss during surgery, RTA, Excessive diarrhoea/vomiting, massive burns, acute pancreatitis, Heat exhaustion. Dry skin, sunken eyes, dry mouth signs of dehydration) present
Cardiogenic shock	<ul style="list-style-type: none"> • Typical features of shock • How to differentiate? Take the concept of CVP first. CVP reflects the amount of blood returning to the heart and the ability of the heart to pump the blood back into the arterial system. • Raised JVP, why does JVP rises in Cardiogenic and not in other types of shock? Because cardiogenic shock results from cardiac failure. Heart loses its ability to pump the blood out of heart. Which results in stasis of blood inside the heart and resulting in backflow of blood towards vena cava. That ultimately results in raised CVP. • And why does it not rise in other types of shock? We know that there is already hypoperfusion of organs, and to meet the needs of the organs heart tries to compensate by increasing contractility and HR. So, blood doesn't stay in heart as there's no problem with the heart itself.
Distributive shock	<p>It includes Anaphylactic, Spinal or Neurogenic and Septic shock</p> <ul style="list-style-type: none"> • <u>Septic shock:</u> Elevated serum lactate > 2mmol/L or > 18 mg/dl • Reduction in SBP 40% from baseline • Cardiac output in septic shock only increase in early stage slightly then decreases later). • All the features of shock mentioned earlier. <u>How to differentiate from other types?</u> • Warm extremities due to release of inflammatory mediators. • Temperature > 38°C or < 36°C. WBCs >14000 or < 4000 • Lactic acidosis resulting in increased lactate levels (normal lactate 0.5-1mmol or 18mg/dl). This is due to Anaerobic glycolysis. • Cardiac output initially increases then decreases, overall CO is raised in septic shock. • <u>Anaphylactic Shock:</u> Allergic reaction results from activation of hypersensitivity reaction. Involves IgE Ab mainly. Results from Mismatched blood transfusion,

	<p>Drug allergies, Food allergy, Snake venom, Insect bite. How to differentiate? Signs and symptoms</p> <ul style="list-style-type: none"> Itching, sweating, diarrhoea and vomiting, erythema, urticaria, oedema, Wheeze, laryngeal obstruction, cyanosis. Increased CO <p>Neurogenic Shock: Same features of Shock</p> <ul style="list-style-type: none"> Results from CVA, Brainstem injury, Spinal cord injury. And results in loss of sympathetic supply to periphery resulting in loss of vasomotor tone Now how to differentiate? Look for Bradycardia + Loss of vasomotor tone
Obstructive shock	<ul style="list-style-type: none"> Indirect pump failure occurs i.e., Cardiac function is decreased due to non-cardiac factors like cardiac tamponade, pneumothorax, pulmonary embolism. Cardiac tamponade-Beck's triad = Raised JVP, muffled heart sounds, hypotension Pericardiocentesis through subxiphoid approach is the preferred choice. Sudden chest pain with sudden dyspnoea and collapse indicates pulmonary embolism. Sinus tachycardia is the most important feature of PE on ECG

STAGES OF SHOCK

Compensatory stage	<ul style="list-style-type: none"> In initial stages, shift of aerobic to anaerobic metabolism, elevated lactic acid levels (metabolic acidosis, sympathetic system stimulation causes release of catecholamines - increase cardiac contractility, neurohormonal response → vasoconstriction and blood shunted to vital organs, ↑ glucose and HR. Aldosterone released decreases Urine output (< 30 mL/hr)
Progressive stage	<ul style="list-style-type: none"> Electrolyte imbalance, metabolic acidosis, respiratory acidosis, peripheral edema, hypotension, pallor, cold clammy extremities, irregular tachyarrhythmias and altered mental status
Refractory stage	<ul style="list-style-type: none"> Irreversible cellular and organ damage, impending death.

SUMMARY OF HEMODYNAMIC PARAMETERS

CVP	↑ only in Cardiogenic shock, ↓ in hypovolemic & Distributive shock
JVP	raised in Cardiogenic shock only
PCWP	Pulmonary capillary wedge Pressure – increase in Cardiogenic shock. Dec in other types of shock
Cardiac index	increase in Distributive shock (septic and anaphylactic shock)
TPR/SVR	Total Peripheral resistance/Systemic Vascular Resistance (SVR): increase in Hypovolemic + Cardiogenic shock
Skin Temp	Warm moist in Sepsis, dry warm in neurogenic shock, rest all types – Cold clammy skin

KEY FACTS - SHOCK

- Dec CVP + increase Lactate + dec cardiac output = Hypovolemic shock – cold, clammy skin
- Dec CVP + Inc Lactate + increase Cardiac Output = Septic shock – Warm, moist skin
- Warm skin + dec TPR + increase CO = Anaphylactic shock
- Loss of Vascular tone + dec TPR + dec CO = Neurogenic Shock – bradycardia may be a feature of it.
- O₂ saturation or Mixed Venous O₂ sat (mvO₂): increase in Septic shock.
- Most common manifestation of shock (septic shock): HYPOTENSION
- Activated Protein C Decreases Mortality in sepsis.
- CVP and JVP raised in cardiogenic shock.
- Lactic Acid dilates Arterioles – decrease CO.
- Lactic acid Oxygen debt = 8 Litres
- Typically, an oxygen debt consists of two stages: A fast stage or a lactic debt – the oxygen is used during recovery to re-synthesise fuels used in a lactic energy system, i.e., ATP and Creatine phosphate.
- Alactoid Oxygen debt = 3.5 Litres
- DOC for anaphylactic shock - IM adrenaline, for cardiogenic shock-dopamine, for septic shock -nor adrenaline. Gram +Ve bacteria are most common cause of septic shock.
- For > 30 % blood loss, give crystalloids + blood.
- In 15% blood loss, use 3× Ringer lactate > 3 × Normal saline.

CLASSIFICATION OF HEMORRHAGE

	Class I	Class II	Class III	Class IV
Blood loss (mL)	Up to 750	750-1500	1500-2000	> 2000
Blood loss (% blood volume)	Up to 15 %	15-30 %	30-40 %	>40 %
Heart rate	< 100	>100	>120	>140
Blood pressure	Normal	normal	decreased	decreased
Pulse pressure	normal	decreased	decreased	decreased
Respiratory rate	14-20	20-30	30-40	> 35
Urine output (mL /hr)	>30	20-30	5-15	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Fluid replacement (3: 1 rule)	crystalloid	crystalloid	Crystalloid + blood	Crystalloid + blood

SHOCK COMPARISON

Type of Shock	Causes:	Pathophysiology	Signs and Symptoms
Hypovolemic	Body Fluid Depletion— <ul style="list-style-type: none"> Hemorrhage <ul style="list-style-type: none"> Internal External Dehydration 	Too little blood volume causes a MAP ↓ so that body's need for tissue oxygenation is not met. (↓CO ↓CVP ↓PAP ↓PCWP)	↑ Respirations Weak, rapid pulse ↓ blood pressure ↓ O ₂ saturation Skeletal muscle weakness Cyanotic, cold, clammy skin Changes in H&H Prolonged Capillary Refill ↓ or absent urine output Thirst, agitation, anxiety Confusion, lethargy Pain Respiratory Acidosis ↓ deep tendon reflexes
Cardiogenic	Direct Pump Failure <ul style="list-style-type: none"> MI, Cardiac Arrest Ventricular Dysrhythmia 	Heart cannot contract effectively Fluid volume not affected ↓ CO ↓ Afterload → ↓ MAP (↓ CO ↑ CVP ↑ PAP ↑ PCWP)	Tachycardia Hypotension Tachypnea BP < 90 mm Hg, or 30 mm Hg less than baseline Cold, clammy skin with poor peripheral circulation Continuing chest discomfort Urine output < 30 mL per hour Agitation, restlessness, or confusion Pulmonary Congestion
Distributive	Decreased Vascular Volume or Tone <ul style="list-style-type: none"> Neural Sympathetic stimulation of nerves controlling blood vessels is decreased, smooth vessel muscles relax causing vasodilation Chemical Anaphylaxis Sepsis Capillary Leak Syndrome 	Vasodilation with pooling causes decreased preload and decreases in stroke volume and CO Fluid shifted from central Vascular space Anaphylactic: (↓CO ↓CVP ↓PAP ↓PCWP) Early Sepsis: (↑CO normal or ↑ PAP + PCWP) Late Sepsis: (↓CO ↓CVP ↓PAP ↓PCWP)	Anaphylactic: damage to cells causes release of histamine which dilates vessels and increases capillary permeability causing severe hypovolemia and vascular collapse. Decreased contractility and dysrhythmias occur. Bronchial edema and pulmonary obstruction. Whole body hypoxia. Septic: Associated with DIC. Toxins and endotoxins released into blood cause Systemic Inflammatory Response Syndrome. Metabolism becomes aerobic because of ↓ MAP, clot formation in capillaries and poor cell uptake of O ₂ . Capillary Leak: fluid shift from blood to interstitial space.
Obstructive	Indirect Pump Failure <ul style="list-style-type: none"> Cardiac tamponade Pulmonary embolus 	Cardiac function decreased by non-cardiac factors Total body fluid volume not affected (↓ CO ↑ CVP ↑ PAP ↑ PCWP)	Cardiac tamponade: JVD, Paradoxical Pulse, ↓CO, muffled heart sounds. Pulmonary embolus: sudden onset dyspnea, pleuritic chest pain, apprehension, restlessness, cough, feeling of impending doom, hemoptysis, tachypnea, crackles, S3 or S4, diaphoresis, low grade fever, petechiae on chest and axillae, ↓ SaO ₂

PAST PAPERS BCQs

1. DIC caused by Endotoxin Shock, tissue thromboplastin or tissue factor (factor III) plays key role in DIC
2. Gram + ve bacteria are the most common cause of Septic shock.
3. Difference between septic and hypovolemic shock? Temperature
4. Difference between anaphylactic and hypovolemic shock? Increase Cardiac Output
5. 3rd space fluid loss may occur in acute pancreatitis, surgery, or trauma.
6. Fluid of choice in 3rd space loss is Ringer Lactate > Normal Saline.
7. Scenario of patient with B.P 80/60, dec. CVP, inc. Serum lactate dehydrogenase, tachycardia? Septic shock
8. A student of final year MBBS witnessing surgery for the first time collapsed in OT due to Decrease in peripheral resistance? Vasovagal shock
9. Shock important component? Tissue hypoxia
10. Most important indicator of hypovolemic shock is -- Dec Urine output.
11. Compensation of shock what will decrease? HR. Heart rate will decrease & Urine output will increase
12. A patient came in emergency 2cm water JVP 2L cardiac output, lactate 30 in blood BP 70/30. What type of shock is this? Hypovolemic shock
13. CVP & JVP increases in Cardiogenic shock
14. Systemic vascular resistance increases in Hypovolemic shock & Cardiogenic shock
15. CO increases in Septic and anaphylactic shock
16. Loss of Vasomotor tone + low BP + low HR in: Neurogenic shock
17. In Spinal shock: reflexes may return to normal with time
18. In 10 – 15 % blood loss: use 3 × Ringer Lactate > 3× Normal Saline.
19. Bp falls in class 3 haemorrhage: 1500 – 2000 ml blood loss.
20. Urine output is affected when approx. 2000 ml blood loss occurs
21. Tachycardia is the earliest imp feature of shock.
22. For > 30% blood loss: Blood transfusion is done along with Crystalloids
23. Inc Urine Output is a reliable feature of recovery from shock
24. In uncompensated shock: Acidosis (both Metabolic + Respiratory) occurs
25. In Anaphylactic shock or histamine shock; DOC – I/M ADRENALINE
26. For Cardiogenic shock: DOPAMINE is the DOC
27. For Septic shock: NOR ADRENALINE is DOC
28. In Hypovolemic shock & Unrecordable BP: first use Adrenaline then Dopamine later - when BP is recordable
29. But for Cardiogenic shock with Unrecordable BP always prefer DOPAMINE > DOBUTAMINE
30. Half-life of Dopamine is 2 min. it reaches steady state in 9 min approx.
31. Pale or White infarct occurs in Heart, Kidney & Spleen
32. Red infarct in: Intestine, Testis, Ovaries, Lungs & Liver.
33. Least chances of infarction in Liver
34. Organs with dual blood supply are prone to red infarct (venous occlusion occurs)
35. Pale infarcts are caused by arterial occlusion
36. Pt with Atherosclerosis presented with acute abdomen, on Laparotomy intestine was dark purple, SMA was atherosclerosis, but SMV was patent: diagnosis is WET Gangrene NOT Red infarct because vein is patent
37. Venous thrombosis results in pulmonary embolism
38. Emboli first go to IVC > Rt Atrium
39. Emboli first lodge in: Pulmonary artery or Lung. So, remember the diff b/ w go to and lodge into.
40. Venous thrombi form snake like pattern towards heart and arterial thrombi away from Heart
41. Paradoxical emboli bypasses Lungs by R → L shunt e.g., ASD, Patent Foramen Ovale and enters left heart
42. Obstruction of Medium sized Pulmonary vessels causes: Pulmonary haemorrhage (Not infarction)
43. Only 10 % emboli may cause infarction
44. Pulmonary infarction is Pyramidal shaped with apex toward hilum of lung
45. Lines of Zahn seen in Coralline thrombus > Antemortem or recent thrombi or arterial thrombi
46. Chicken – fat appearance in postmortem clot
47. History of passing CVP, Criminal abortion, Laparoscopy, neck / chest injury → Air Embolism
48. 100 cc air is required for air embolism
49. Fat embolism on autopsy visualized by : Frozen Section + Fat Stain (Sudan Black)
50. Amniotic fluid embolism is most fatal or lethal 20- 40 % mortality risk

51. Arteriolar constriction is protective against edema
52. Inflammation is the MCC of Local edema – allergy may cause local edema as well
53. Most common manifestation of shock (septic shock): HYPOTENSION
54. In 10 – 15 % blood loss: use 3× Ringer Lactate > 3× Normal Saline.
55. Bp falls in class 3 haemorrhage: 1500 – 2000 ml blood loss.
56. Fluid of choice in 3 rd space loss is: Ringer Lactate > Normal Saline.
57. Shock important component? Tissue hypoxia
58. Difference between septic and hypovolemic shock? Temperature
59. Difference between anaphylactic and hypovolemic shock? INCREASE CARDIAC OUTPUT
60. In All types of shock = decrease Cellular oxygenation occurs leading to tissue hypoxia
61. Not frequently related to Embolus: LIQUID
62. Tachycardia is the primary feature of shock
63. In septic shock: Lactate raised > mixed venous O ₂ content
64. Lactate also raised in Hypovolemic shock, so correlate with other features to differentiate it from Septic shock. If Low CO is not mentioned – only Raised Lactate & low BP mentioned → prefer Septic shock.
65. MI – most common cause of cardiogenic shock.
66. Tachycardia, low BP & abdominal distension after laparotomy: HYPVOLEMIC SHOCK
67. Platelets cause: Blood clot retraction
68. Inc Urine output is NOT a feature of Shock
69. Inc CO in anaphylactic shock also
70. Sea diver develops SOB & Joint pain due to: N ₂ bubble – Caisson's disease or decompression sickness
71. Prolonged immobilization is the MCC of DVT formation
72. Endothelial injury is Most imp factor for thrombosis – 1 st step in thrombus formation is endothelial injury
73. Stasis is imp independent factor for thrombosis
74. After surgery, pt presented with Swollen legs, DVT suspected the cause is: STASIS + Hyper-coagulopathy
75. After C section lady dies due to: amniotic fluid embolism
76. Most common inherited thrombotic disorder is: Factor V laden mutation (not simple Factor V – it is LADEN)
77. Factor V def leads to Bleeding, But Factor V LADEN mutation leads to Thrombosis
78. Def of Factor 12 causes thrombosis rather than bleeding
79. Most common acquired thrombotic disorder is: Antiphospholipid syndrome APLS
80. Most common inherited coagulopathy: Von Willebrand's disease
81. Activated Protein C dec Mortality in sepsis
82. Edema occurs due to Decrease Capillary oncotic pressure, Inc Capillary Hydrostatic pressure & increase Capillary permeability
83. Low protein & Low cell count in Transudate
84. Most extensive necrosis + death with which type of embolism: Amniotic fluid embolism - ruptured Uterine veins
85. Lymphatics return the tissue fluid
86. Platelet adherence is earliest step in haemostasis / formation of thrombus
87. For Fat embolism: h/o long bone fracture, also called marrow embolism.
88. Death occurs in fat embolism – 72-96 hrs post trauma
89. Atheroma is the most imp cause of infarction (pale infarct) in Solid organs
90. Emboli may cause red infarction and thrombi (by atheroma) may cause Pale infarction
91. Dec Venous Pressure can't cause Edema
92. In Sea divers: Oxygen toxicity causes death by SIZEURES
93. Systemic arterial thromboembolism occurs due to: Left Ventricle Mural thrombus
94. Endothelial injury, stasis & hypercoagulable states is the correct sequence of thrombus formation
95. For Valvular damage leading to Micro emboli sequence is as follows:
96. Damaged Valve, Thrombus, Bacteraemia, Perforation – (D -- TBP)
97. Emboli is the most common complication of: DVT
98. Peripheral claudication is a feature of Peripheral arterial disease
99. IL – 6 is the last mediator of endotoxic shock
100. 1 st mediator of septic shock is: TNF. The sequence is: TNF – IL – 1 – IL – 6
101. Schwartz phenomena seen in endotoxic shock
102. Generalized Edema Is Called Anasarca
103. CHF may cause dependant edema

104.DVT source is: Popliteal Vein most commonly
105.DVT causing Pulmonary embolism: the source most commonly is Femoral Vein
106.Tissue factor / Factor III plays main role in DIC – most common coagulopathy in Trauma
107.Factor 10 = Stuart power factor & Factor 7 = Stable factor
108.Factor 12 = Hageman factor – activates Pre – kallikrein to Kallikrein which converts High Molecular weight Kininogen to Bradykinin. Kallikrein also activates Plasminogen to Plasmin
109.Platelets function by: ADP & Thromboxane A ₂ .
110.Platelets change shape from flat to Spherical when activated.
111.Aspirin partially inhibits thromboxane A ₂ (TXA)
112.Edema in Nephrotic syndrome or liver Cirrhosis = due to Low Albumin or low Plasma Colloid osmotic pressure
113.Edema in nephrotic syndrome: Low albumin + salt retention > Low Albumin
114.Edema in HTN or CHF: Due to Inc Hydrostatic pressure.
115.Edema in inflammation: increase Vascular permeability
116.Edema worsens in Heart Failure (CCF) due to Salt & Water retention
117.Edema in nephritic syndrome due to: Salt and water retention
118.Thromboembolism is the cause of death in Pulmonary embolism
119.Angioneurotic edema is linked with IgE

NEOPLASIA

Neoplasia	An abnormal mass, the growth of which exceeds & uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change. The change may be genetic change, autonomous or clonal.
Components of tumour	<ol style="list-style-type: none"> Parenchyma- neoplastic cells: Epithelial origin / Mesenchymal origin Non neoplastic stroma: Supportive connective tissue and blood Vessels and cells of immune system <p>Desmoplasia is the Abundant fibro collagenous Stroma in tumour—hard consistency “scirrhus”. It is non-Neoplastic growth of connective tissue around tumour e.g., in Breast cancer.</p>

NOMENCLATURE

Benign tumours (-Oma as suffix)	Oma as suffix = benign neoplasm	
	Epithelial tumours	<ul style="list-style-type: none">• Adenoma: tumour forming glands• Papilloma: tumour with finger like projections• Papillary cystadenoma: papillary and cystic tumour forming glands.• Polyp: a tumour that projects above a mucosal surface
	Mesenchymal tumours	<ul style="list-style-type: none">• Chondroma: cartilaginous tumour• Fibroma: fibrous tumor• Osteoma: bone tumour
Malignant tumours	Carcinomas	Carcinomas are epithelial tumours. <ul style="list-style-type: none">• Adenocarcinoma: gland forming tumour• Squamous cell carcinoma: squamous differentiation• Undifferentiated carcinoma: no differentiation Note: carcinomas can arise from ectoderm Mesoderm, or endoderm
	Sarcomas	Sarcomas are mesenchymal tumours (connective tissue origin) <ul style="list-style-type: none">• Chondrosarcoma: cartilaginous tumour• Fibrosarcoma: fibrous tumour• Osteosarcoma: bone tumour
Benign Tumour		Malignant Tumour
Well – Circumscribed & Encapsulated		Poorly Circumscribed & Encapsulated
No Local invasion; except a few		Locally invasive
Slow – growing & Smaller size		Slow to rapid growth & Large at presentation
Function of organ may be retained		Loss of function in Poorly differentiated tumours
Misnomers	<ul style="list-style-type: none">• These tumours have – Oma as suffix but they are malignant, not benign.• Hepatoma: malignant liver tumour• Melanoma: malignant skin tumour• Seminoma: malignant testicular tumour• Lymphoma: malignant tumour of lymphocytes	
Tumours with Mixed differentiation	<ul style="list-style-type: none">• Mixed tumours: e.g., pleomorphic adenoma of salivary gland and Carcinosarcoma• Teratoma: Tumour comprised of cells from more than one germ layer Arise from totipotent cells (usually gonads). Benign cystic teratoma of ovary is the most common Teratoma	
Aberrant differentiation	Not true neoplasms, they include: <ol style="list-style-type: none">1. Hamartoma: disorganized mass of tissue whose cell types are Indigenous to the site of the lesion2. Choriostoma: ectopic focus of normal tissue (heterotopia) i.e., normal tissue at a different site	

NATURAL HISTORY OF MALIGNANT TUMOURS

- Malignant change in the target Cell, referred to as Transformation.
- Growth of the transformed cells
- Local invasion: invasion of capsule and basement membrane
- Distant metastases are the reliable feature of malignancy, spreads by Hematogenous/Lymphatic route and seedling into body cavities.

Differentiation	<ul style="list-style-type: none"> Differentiation means how well the tumours cells resemble their parent's cells of origin. Benign tumours are well differentiated. Poorly differentiated malignant tumours usually Have worse prognosis. <table> <tr> <td>Well differentiated neoplasm</td><td> <ul style="list-style-type: none"> Resembles mature cells of tissue of origin. > 75 % differentiation </td></tr> <tr> <td>Moderately differentiated neoplasm</td><td> <ul style="list-style-type: none"> moderately resemble the cell of tissue of origin. 50 – 75 % differentiation </td></tr> <tr> <td>Poorly differentiated neoplasm</td><td> <ul style="list-style-type: none"> Composed of primitive cells with little Differentiation 25 – 50 % differentiation </td></tr> <tr> <td>Undifferentiated or anaplastic</td><td> <ul style="list-style-type: none"> < 25 % differentiation or > 75% undifferentiated cells </td></tr> </table>	Well differentiated neoplasm	<ul style="list-style-type: none"> Resembles mature cells of tissue of origin. > 75 % differentiation 	Moderately differentiated neoplasm	<ul style="list-style-type: none"> moderately resemble the cell of tissue of origin. 50 – 75 % differentiation 	Poorly differentiated neoplasm	<ul style="list-style-type: none"> Composed of primitive cells with little Differentiation 25 – 50 % differentiation 	Undifferentiated or anaplastic	<ul style="list-style-type: none"> < 25 % differentiation or > 75% undifferentiated cells
Well differentiated neoplasm	<ul style="list-style-type: none"> Resembles mature cells of tissue of origin. > 75 % differentiation 								
Moderately differentiated neoplasm	<ul style="list-style-type: none"> moderately resemble the cell of tissue of origin. 50 – 75 % differentiation 								
Poorly differentiated neoplasm	<ul style="list-style-type: none"> Composed of primitive cells with little Differentiation 25 – 50 % differentiation 								
Undifferentiated or anaplastic	<ul style="list-style-type: none"> < 25 % differentiation or > 75% undifferentiated cells 								
Anaplasia	The Total lack of differentiation, Pleomorphism in Size & Shape, Abnormal nuclear morphology, Hyperchromasia, High N/C ratio, Chromatin clumping and Prominent nucleoli, high Mitotic rate.								
Dysplasia	<ul style="list-style-type: none"> Recognized by loss of polarity and cellular architecture. In dysplasia, some but not all the features of Malignancy are present. Dysplasia may develop into malignancy e.g., Uterine cervix or Colon polyps. Dysplasia may NOT develop into malignancy also. Dysplasia is divides into 3 Grades as: low-grade, moderate or high-grade. <table> <tr> <td>Mild dysplasia</td><td>atypia involves less than one - third of mucosal thickness</td></tr> <tr> <td>Moderate dysplasia</td><td>involves one to two – thirds of thickness (1/3rd to 2/3rd)</td></tr> <tr> <td>Severe dysplasia</td><td>High grade dysplasia involves > 2/3rd of thickness of epithelium</td></tr> </table>	Mild dysplasia	atypia involves less than one - third of mucosal thickness	Moderate dysplasia	involves one to two – thirds of thickness (1/3 rd to 2/3 rd)	Severe dysplasia	High grade dysplasia involves > 2/3 rd of thickness of epithelium		
Mild dysplasia	atypia involves less than one - third of mucosal thickness								
Moderate dysplasia	involves one to two – thirds of thickness (1/3 rd to 2/3 rd)								
Severe dysplasia	High grade dysplasia involves > 2/3 rd of thickness of epithelium								
Carcinoma in Situ	It has all features of malignant tumour except that it is limited by Basement membrane. CIS invades Basement membrane to becomes invasive & spreads to surrounding tissues + distant organs.								
Tumour Growth rate	<ol style="list-style-type: none"> Doubling time of tumour cells Lengthens as tumour grows: <ul style="list-style-type: none"> 30 doublings (10⁹cells) = 1g takes (months to years). 10⁹ more doublings (1 kg) = lethal burden Fraction of tumour cells in replicative pool: <ul style="list-style-type: none"> May be only 20% even in rapidly growing tumours. Tumour stem cells Rate at which tumour cells are shed or lost -- Apoptosis and Maturation rate. Implications for therapy 								
Invasion & Metastasis	<p>For malignant cells to establish a metastasis, a Number of steps are required.</p> <ul style="list-style-type: none"> Invasion of the basement membrane underlying the Tumour. Movement through the extracellular matrix. Penetration of the vascular or lymphatic channel. Survival and arrest within the circulatory blood and Lymph. Exit from circulation (extravasation) into new tissue site. <table> <tr> <td>Invasion</td><td>Metastasis</td></tr> <tr> <td> <ul style="list-style-type: none"> Local spread of malignant tumour by invasion of BM infiltration or destruction of adjacent tissue A type of local seedling Tumours that locally invade but rarely metastasize are Basal cell carcinoma > Ameloblastoma </td><td> <ul style="list-style-type: none"> A life-threatening event involving transfer of tumour cells at distant locations (organs) through blood, lymphatics or seedling into body cavities. Loss of E-cadherin → loss of cell-cell contacts leads to metastasis e.g., in Gastric cancer </td></tr> </table>	Invasion	Metastasis	<ul style="list-style-type: none"> Local spread of malignant tumour by invasion of BM infiltration or destruction of adjacent tissue A type of local seedling Tumours that locally invade but rarely metastasize are Basal cell carcinoma > Ameloblastoma 	<ul style="list-style-type: none"> A life-threatening event involving transfer of tumour cells at distant locations (organs) through blood, lymphatics or seedling into body cavities. Loss of E-cadherin → loss of cell-cell contacts leads to metastasis e.g., in Gastric cancer 				
Invasion	Metastasis								
<ul style="list-style-type: none"> Local spread of malignant tumour by invasion of BM infiltration or destruction of adjacent tissue A type of local seedling Tumours that locally invade but rarely metastasize are Basal cell carcinoma > Ameloblastoma 	<ul style="list-style-type: none"> A life-threatening event involving transfer of tumour cells at distant locations (organs) through blood, lymphatics or seedling into body cavities. Loss of E-cadherin → loss of cell-cell contacts leads to metastasis e.g., in Gastric cancer 								
Pathways of spread	<ul style="list-style-type: none"> Lymphatics route: used by carcinomas mostly e.g., breast & colon CA, Papillary thyroid CA, Melanoma, Sentinel lymph node is the first lymph node to receive from a primary tumour. Uterine cancer spreads least via this route Hematogenous route: used by sarcomas, 4 carcinomas spread by this route (Thyroid Follicular CA, Choriocarcinoma, RCC, HCC) invasion of vein is imp in RCC and HCC Direct seedling into body cavities/surfaces: Ovarian carcinoma spreads via Peritoneum > Lymph node 								

	Endometrial cancer mostly spreads via direct penetration into myometrium
Sites of Metastasis	<p>Metastasis is more common than a primary cancer in the following sites:</p> <ul style="list-style-type: none"> • Lymph node – (e.g., metastatic breast and lung cancer most common) • Lungs: (e.g., Metastatic breast cancer most common) • Liver: (e.g., metastatic lung cancer & Colorectal cancer are common) • Bone: (e.g., Metastatic breast cancer is most common) • Brain: (e.g., Metastatic lung cancer is most common) • Liver & Lungs are Overall most common sites of Metastasis after lymph nodes. • Ovarian carcinoma metastasizes via: Peritoneum > Lymph Nodes • Endometrium cancer spreads by Direct penetration commonly and least route followed by it is via Lymphatics. • Colorectal cancer metastasized firstly into: Lymph Nodes • Top three sites for Gynaecological malignancy: Endometrium > Ovary > Cervix • Prostate Cancer is most common in Men while Breast cancer most common in Females. • Highest Mortality in both sexes by: Lung CA
Key Facts	<ul style="list-style-type: none"> ❖ Diagnostic feature of malignancy: Metastasis > invasion > pleomorphism > high n/c ratio ❖ Microscopic feature of malignancy: invasion ❖ Microscopic feature of premalignant lesion: pleomorphism ❖ Microscopic feature of premalignant condition: N/C ratio ❖ Histopathological feature of malignancy: invasion of basement membrane (BM) ❖ Loss of E – cadherin is linked to spread of tumour i.e., metastasis

PREDISPOSING FACTORS FOR CANCER

Age	Most cancers occur in persons > 55 years. Childhood cancers are Leukemias, CNS neoplasms and Bone tumours
Genetic predisposition	<p>Familial cancer syndromes: Early onset, ≥ 2 primary relatives with the cancer, Multiple or bilateral tumours</p> <p>Polymorphisms that metabolize procarcinogens, e.g., nitrites</p>
Non-hereditary conditions	<p>Chronic inflammation: Chronic atrophic gastritis predisposes to gastric adenocarcinoma.</p> <p>Precancerous conditions: Chronic ulcerative colitis, Atrophic gastritis of pernicious anaemia, leukoplakia.</p>

GRADING VS STAGING

GRADE	STAGE
<p>Grading is the histological character of tumour compared to original cell structure.</p> <p>Grading done on 1-3 or 4 scale.</p> <p>It depends upon amount of mitosis at atypia.</p> <p>High grade means Poorly differentiated; worse prognosis as cells are more different in structure and function from normal cells.</p> <p>Well differentiated = low grade; better prognosis</p>	<p>Staging refers to the extent of disease in the body based on invasion and metastasis (from Stage I-IV)</p> <p>TNM = Tumour, node, metastasis.</p> <p>Most used system for staging is TNM.</p> <p>Prognosis depends mainly on Staging.</p> <p>Higher stage means worse prognosis.</p>
Grading	<ul style="list-style-type: none"> • Grade 1: cells differ slightly from normal cells, > 75% differentiated. • Grade 2: moderately differentiated, 50-75% differentiated. • Grade 3: very abnormal poorly differentiated cells i.e., severe dysplasia, 25-50% differentiation • Grade 4: immature cells, anaplastic, undifferentiated totally (> 75%), < 25% differentiation
Staging	<ul style="list-style-type: none"> • Stage 0 = Carcinoma in original place • Stage 1 = localized tumour growth, limited to tissue of origin • Stage 2 = limited local spread • Stage 3 = extensive regional and local spread • Stage 4 = distant metastasis

Hallmarks of Cancer	<ul style="list-style-type: none"> Transformation & Progression of Cancer or Hallmarks of Cancer includes: <ol style="list-style-type: none"> 1. Self-sufficiency in growth signals: by producing own growth factors and paracrine factors. 2. Insensitivity to growth-inhibiting signals: RB & P53 involved as explained below 3. Evasion of apoptosis (P53, BCL, MYC involved) 4. Defects in DNA repair: "Spell checker. HNPCC (Hereditary Non-Polyposis Colon Cancer): TGF-B, B-catenin, Xeroderma Pigmentosum (UV fixing gene), Ataxia Telangiectasia - ATM gene, Bloom Syndrome due to defective helicase. 5. Limitless replicative potential: Telomerase activity 6. Angiogenesis: via VEGF & PDGF 7. Invasive and Metastatic ability
----------------------------	--

Molecular basis of cancer	<ol style="list-style-type: none"> 1. Non-lethal genetic damage 2. A tumour is formed by the clonal expansion of a single precursor cell (monoclonal) 3. Four classes of normal regulatory genes are; <ol style="list-style-type: none"> a. Proto-oncogenes b. Oncogenes → Oncoproteins c. DNA repair genes d. Apoptosis genes 4. Carcinogenesis is a multistep process
Carcinogenesis is multi-step	<ul style="list-style-type: none"> • no single oncogene causes cancer. • Both oncogenes and several tumour suppressor genes must be involved • gatekeeper/caretaker concept gatekeepers = oncogenes and tumour suppressor genes • caretakers: DNA repair genes • tumour progression by angiogenesis • heterogeneity from original single cell
Role of RB and P53 gene	<p>The most prominent brakes are Rb & P53 gene.</p> <ol style="list-style-type: none"> 1. Retinoblastoma gene (Rb) (Gatekeeper or Governor of Genome) <ul style="list-style-type: none"> • Direct regulator of the cell division cycle. RB transduces growth-inhibitory signals and decides whether a cell should proceed Through its growth-and-division cycle. • Defects in the RB pathway function → Persistent cell proliferation. 2. P53 pathways: Guardian of the genome <ul style="list-style-type: none"> • TP53 receives inputs from stress and abnormality sensors that function within the Cell's intracellular operating systems. • TP53 can Halt further cell-cycle progression and Trigger apoptosis. • Mutation in P53 → increases cell survival – tumour formation
Proto-oncogenes	Normal cellular genes whose products promote cell Proliferation e.g., growth factors
Oncogenes	Mutated or over expressed versions of proto-oncogenes That function autonomously having lost dependence on normal growth Promoting signals. Viruses cause Cancer by using Oncogenes.
Oncoproteins	<ul style="list-style-type: none"> • A protein encoded by an oncogene that drives increased cell proliferation. • Mutations in Oncogene result in Dominant gain of function • Mutations in Tumour Suppressor genes result in Recessive Loss of function

Oncogenes	Tumour suppressor genes
<ul style="list-style-type: none"> • Mutation in one of 2 alleles is sufficient. • Gain of function of protein signals cell division • Mutation arises in somatic cells, not inherited 	<ul style="list-style-type: none"> • Both alleles must be affected • Loss of function of protein • Mutation present in germ cell (inherited) or somatic

PROTO-ONCOGENES / ONCOGENES & TUMOUR SUPPRESSOR GENES ROLE IN MALIGNANCY

- Protooncogenes may encode growth factors, growth factor receptors, signal transducers or cell cycle components.
- KRAS, RET, MYC, KIT, BCL – 2, BRAF, BCR – ABL, JAK – 2 are all Protooncogenes

Growth Factors

involved in Glioblastoma and sarcomas.

Growth Factors Receptors

Receptor tyrosine kinases can be constitutively activated by many Mechanisms like:

- Point mutations: in Lung adenocarcinoma.
- Gene amplifications: in Breast Carcinoma
- RET is receptor tyrosinase kinase involved in: Medullary + Papillary thyroid Ca, Pheochromocytoma.

Signal Transduction Proteins

- KRAS mutations – Pancreatic adenocarcinoma, cholangiocarcinoma, Colorectal Ca**
- BRAF mutations – Hairy cell leukaemia, melanomas
- PI3K mutations – Breast carcinoma
- BCR – ABL: Non receptor tyrosine kinase – CML > ALL**

RAS mutation:

- Point mutations in RAS family of genes constitute the most common abnormality involving proto-oncogenes. 15- 20% of all human tumours express RAS mutation.
- RAS genes are of 3 types – HRAS, KRAS, NRAS.
- RAS proteins are members of a family of membrane associated small G protein.
- Mutations markedly reduce the GTPase activity of RAS.

Transcription Factors

- C - MYC translocation – Burkitt's lymphoma
- N - MYC amplification: Neuroblastoma
- L – MYC amplification: small cell LUNG Carcinoma
- C – kit mutation: Gastrointestinal stromal tumours i.e., GIST.

Cell Cycle Regulators

There are two main cell cycle checkpoints.

- G1/S transition
- G2/M transition

These are tightly regulated by a balance between growth promoting and growth suppressing factors as well as by sensors of DNA damage.

When activated, these DNA damage sensors arrest cell cycle Progression and if cell damage cannot be repaired initiate apoptosis.

Defects in G1/S checkpoint are more important in cancer as they lead to dysregulated growth and mutator phenotype. Mutations that affect G1/S checkpoint can be broadly divided into

- Gain of function mutations of cyclin D and CDK4 oncogenes that Promote G1/S progression. Examples – lymphoma, sarcomas.
- Loss of function mutations in tumour suppressor genes that inhibit G1/S progression. Examples --- Pancreatic Carcinomas, Glioblastoma, ALL

Tumour suppressor genes**Kundson's 2 hit hypothesis:**

2 alleles of tumour suppressor genes must be lost for tumour causation.

Tumour suppressor gene	Associated Cancers
RB	Retinoblastoma, osteosarcoma
P53	Involved in most cancers > 50 %, (P16 INK 4a) GIT, breast cancers
WT-1	Wilm's tumour
TGF-β	Colon cancer
E-cadherin	Diffuse gastric cancer
NF 1, 2	Neurofibromatosis
APC/β-Catenin	GI adenocarcinoma, melanoma
SMAD-4	Pancreatic adenocarcinoma
PTEN	Endometrial, breast and prostate cancer
BRCA-1, BRCA-2	Breast cancer
KLF-6	Prostate cancer

Oncogenic microbes	Viruses cause cancer by: using oncogenes > alteration in proto-oncogenes > altered protein synthesis. Viruses along with other microbes; bacteria and parasites linked to malignancies.
EBV	Burkitt lymphoma, Hodgkin lymphoma, Nasopharyngeal Ca, primary CNS Lymphoma
HBV, HCV	HCC
HHV-8	Kaposi sarcoma
HTLV-1	Adult T cell leukaemia/lymphoma
H pylori	Gastric cancer and MALTOMA
Liver fluke	cholangiocarcinoma
Schistosoma haematobium	Squamous cell carcinoma of bladder

CHEMICAL CARCINOGENESIS

Concept	<ul style="list-style-type: none">initiation and promotion are two imp steps:initiation/promotion concept: both initiators + promoters are needed for carcinogenesis. Neither can cause cancer by itself.i. Initiators (carcinogens) cause mutations by binding electrophile region. initiators produce memory and are irreversible.ii. Promoters are not carcinogenic by themselves, and must take effect after initiation, not before. promoters enhance the proliferation of initiated cells (clonal expansion). Promoters are reversible.	
Initiators	Direct	Alkylating agents cause Leukaemia / Lymphoma, B-Propiolactone, Dimethyl sulphate. Diepoxy butane, Anticancer drugs (cyclophosphamide, Chlorambucil, Nitrosoureas, and others), Acylating Agents (1-Acetyl-imidazole, Dimethylcarbamyl chlorides)
	Pro-carcinogens	Polycyclic and Heterocyclic Aromatic Hydrocarbons, Aromatic Amines, Amides, ▪Azo Dyes → Bladder Ca Natural Plant and Microbial Products: Aflatoxin B1 → Hepatomas, Griseofulvin → Antifungal, Betel nuts → Oral SCC
promoters	They include hormones, phorbol esters (TPA), activate kinase c, phenols and drugs. initiated cells respond and proliferate faster to promoters than normal cells	
Carcinogen	Associated cancers	
Tobacco smoke	Lung Cancer, Bladder Ca, Oesophageal Ca, Cervix Ca, RCC, tar is carcinogenic -- not nicotine	
Ethanol	HCC, oesophageal SCC, Breast Cancer	
Nitrosamines and amides (tar)	Stomach cancer, most known carcinogen	
Asbestos	Bronchogenic Cancer > Mesothelioma	
Vinyl chloride	Hepatic angiosarcoma	
Nickel	Lung CA > Nose Cancer	
Chromium	Lung CA	
Cadmium	Prostate CA	
Radon	2 nd leading cause of lung cancer	
Arsenic	Hepatic angiosarcoma > Skin cancer	
Others	Insecticides, fungicides, polychlorinated biphenyls (PCBs)	

RADIATIONS AS CARCINOGENS

UV radiations	BCC, SCC, MM (malignant melanoma)
Ionizing radiations (e.g., Photons)	Hematopoietic and Thyroid (90%, over 15years exposure) tumors in fallout victims Solid tumors are either less susceptible or require a longer latency period than leukaemia/lymphoma. BCCs: in Therapeutic Radiation.
Key Facts	<ul style="list-style-type: none"> Radiation causes cancer via proto-oncogene. Radiations cause protein damage which in turn causes oncogenesis: P53. Virus cause cancer in human by modifying proto-oncogene > altering protein synthesis

LABORATORY DIAGNOSIS OF CANCER

MORPHOLOGICAL METHODS	<ol style="list-style-type: none"> 1. Histological examination: tissue from surgical excision or Biopsy <ul style="list-style-type: none"> • Histopathological Exam is for definitive diagnosis & Gold standard for tumour diagnosis. • Sample for Histological exam from: Excision biopsy, Incision biopsy, Punch biopsy, Fine needle aspiration biopsy, Endoscopic biopsy and Frozen sections 2. Cytological examination: pleural effusion, fine needle Aspiration biopsy, Pap's smear 3. Immunohistochemistry or immunocytochemistry: For determination of site of origin of metastatic tumour, categorization of undifferentiated neoplasm, determination of molecules having prognostic or therapeutic significance. 4. Flow cytometry 5. Tumour markers 6. Molecular diagnosis: PCR – based techniques, Hybridization methods, molecular cytogenetics methods. 7. Molecular profiling of tumours 8. Whole genome sequencing
Fine needle aspiration cytology	<ul style="list-style-type: none"> • Aspiration of cells from a mass, Examination of the smear Used most commonly with readily palpable Lesions affecting the breast, thyroid, lymph Nodes, and salivary glands. • Modern imaging techniques permit extension of the method to deeper structures, such as the liver, pancreas, and pelvic lymph nodes
Cytological smears (Pap smear)	<ul style="list-style-type: none"> • Has been used widely for discovery of carcinoma of the Cervix. • Used to investigate Endometrial carcinoma, Bronchogenic carcinoma, Bladder and prostate tumours, Gastric carcinomas. • Identifying tumour cells in Abdominal, pleural, joint, and cerebrospinal fluids • Neoplastic cells are less cohesive than others, so they shed into fluids or secretions → evaluated for features of Anaplasia
Immuno-cytochemistry	<ul style="list-style-type: none"> • It offers a powerful adjunct to routine histologic Examination. • Detection of cytokeratin → points to a diagnosis of undifferentiated carcinoma rather than large Cell lymphoma. • Detection of prostate-specific antigen (PSA) in Metastatic deposits for Definitive diagnosis of a Primary tumour in the prostate. • Immunocytochemical detection of estrogenic Receptors: prognostication and directs Therapeutic intervention in breast cancers.
Flow cytometry	It Is used routinely in the classification of Leukemias and lymphomas. Fluorescent antibodies against cell surface Molecules and differentiation antigens are Used to obtain the phenotype of malignant Cells.
MOLECULAR DIAGNOSIS	<ul style="list-style-type: none"> • For Diagnosis of malignancy- Because each T and B cell exhibits unique rearrangement of its Antigen receptor genes, polymerase chain reaction (PCR)-based Detection of T cell receptor or immunoglobulin genes allows Distinction between monoclonal (neoplastic) and polyclonal (reactive) proliferations. • Many hematopoietic neoplasms, as well as a few solid tumours, are Defined by particular translocations, so the diagnosis can be made by detection of such translocations.

FISH & PCR	<p>Fluorescence in situ hybridization (FISH) or PCR analysis:</p> <ul style="list-style-type: none"> • For Micro deletions, translocations and telomere alterations • Detect Translocations characteristic of Ewing sarcoma and several leukaemia's and lymphomas. • PCR-based detection of BCR-ABL transcripts: for diagnosis of chronic Myeloid leukaemia. • To detect Amplification of oncogenes such as HER2/NEU And N MYC, which provide prognostic and Therapeutic information for breast cancers and Neuroblastomas. • Detection of minimal residual disease Detection of BCR-ABL transcripts by PCR assay Gives a measure of residual disease in patients Treated for chronic myeloid leukaemia. • Detection of microsatellite repeats. Mutation detection by allele-specific
Genomic analysis	<p>Recent results from genomic analyses Individual tumours can contain from a handful of somatic Mutations (certain childhood leukaemia's) to tens of thousands of Mutations.</p> <p>The highest mutational burden being found in cancers Associated with mutagen exposure, such as lung cancer and skin Cancer.</p> <p><u>Two types of mutations:</u></p> <p>Those that subvert normal control of cell proliferation, Differentiation, and homeostasis → driver mutations because They may drive the neoplastic process and hence could be Therapeutic targets.</p> <p>Those that have no effect on cell phenotype → passenger Mutations. Often much more numerous than driver mutations. Result from genomic instability of cancer cells</p>
Microarray	used to detect gene expression like fingerprints, likely to replace histopathological exam in future.
Karyotyping	<ul style="list-style-type: none"> • By using fluorochromes and computer-Generated signals, the entire human genome can be visualized. It detects all types of chromosomal Rearrangements in tumour cells. • It can also detect the origin of Unidentified chromosomes, called marker Chromosomes, seen in many Hematopoietic malignancies.
QUICK RECAP	<ul style="list-style-type: none"> • Several sampling approaches exist for the diagnosis of tumours: Excision Biopsy, Fine-needle aspiration Cytological smears. • Immunohistochemistry and flow cytometry studies help in the diagnosis and Classification of tumours, because distinct protein expression patterns define Different entities. • Proteins released by tumours into the serum, such as PSA, can be used to screen Populations for cancer and to monitor for recurrence after treatment. • Molecular analyses are used to determine diagnosis, prognosis, the detection of Minimal residual disease, and the diagnosis of hereditary predisposition to cancer. • Molecular profiling of tumours by cDNA arrays and sequencing can determine Expression of large segments of the genome and catalogue all the mutations in the Tumour genome and thus may be useful in molecular stratification of otherwise Identical tumours or those of distinct histogenesis that share a mutation for the Purpose of treatment and prognostication. • Translocations and inversions occur in most lymphomas/leukaemia's

CHROMOSOMAL TRANSLOCATION	ASSOCIATED DISORDER
t (9;22) – Philadelphia chromosome	CML (BCR-ABL hybrid)
t (8;14)	Burkitt's lymphoma (C-MYC activation)
t (14;18)	Follicular lymphoma (BCL-2 activation)
t (15;17)	M3 type of AML (APL) responsive to all trans retinoic acid
t (11;22)	Ewing's sarcoma
t (11;14)	Mantle cell lymphoma

TUMOUR MARKERS

- Biochemical indicators of tumour, contributing to the detection of cancer.
- Useful in determining the effectiveness of therapy and recurrence.
- Helpful in diagnosis of tumour and differentiating it from normal tissue
- These chemicals also can be stained by immunochemical methods in tissue (e.g., NSE)

Types	Examples & Associated Cancers
Hormones	<ul style="list-style-type: none"> • HCG (Gestational trophoblastic disease, Gonadal germ cell tumours), normally raised in pregnancy. • Calcitonin (medullary thyroid cancer), Catecholamines (Pheochromocytoma) • Hormones are linked to paraneoplastic syndromes e.g., ACTH (Cushing syndrome, in small cell lung CA)
Enzymes	<ul style="list-style-type: none"> • Prostate specific acid phosphatase (PSA) – Prostate cancer, also raised in BPH and prostatitis. • Neuron specific enolase (NSE) – raised in neuroblastoma and small cell lung cancer. • LDH – linked to lymphoma and Ewing's sarcoma, to assess the tumour burden
Tumour associated Proteins	<ul style="list-style-type: none"> • CA-125, CA 15-3 and CA 19-9 are Glycoproteins. • CA-125 – linked to ovarian cancer, also raised in menstruation, pregnancy and peritonitis. • CA 15-3 – Breast cancer • CA 19-9 – Pancreatic adenocarcinoma, gallbladder and Colon cancer, breast cancer • CD 30 – Hodgkin's lymphoma • CD 25 – hairy cell leukaemia, adult T-cell leukaemia • CD 10 – ALL (pre-B cell marker) • CD 19, 20 – mature B cell marker
Oncofoetal proteins/Ag	<ul style="list-style-type: none"> • Alpha feto-protein (AFP) – raised in HCC, Embryonal cell carcinoma (Yolk sac tumour), cirrhosis, hepatitis. • Carcinoembryonic antigen (CEA) – adenocarcinoma of colon, pancreas, breast, lung, ovary • CEA also raised in non-neoplastic conditions e.g., pancreatitis, hepatitis, IBD, Smoking
NOTE	<ul style="list-style-type: none"> • AFP, HCG, PSA, CEA, CA 15-3, CA 19-9, CD10 are important for exam

Immunocytochemical stain	Normal tissue Expression	Tumour association (+Ve in)
Cytokeratin	All epithelial cells	Carcinomas e.g., SCC
Vimentin	Present on Mesenchymal cells, +Ve in Sarcomas, RCC, mesothelioma, uterine CA	
Desmin	Muscle cells	Rhabdomyosarcomas, leiomyomas
Neurofilament	CNS, PNS neurons, neural crest derivatives	Neuroblastoma, pheochromocytoma
Glial fibrillary acidic protein	GFAP normally present on Glial cells	Astrocytoma's, ependymomas
Synaptophysin	+Ve in salivary gland tumours, larynx CA and tongue CA	
Chromogranin	+Ve in carcinoid tumour (syndrome)	
S-100	+Ve in melanoma, schwannoma, tumour of fat cells, macrophages, dendritic cells	
5-HIAA	5 Hydroxy indole acetic acid; +Ve in carcinoid syndrome	

PARANEOPLASTIC SYNDROMES (PNS)

- They are non-metastatic Manifestations of malignancies.
- Complexes of Symptoms that occur alongside the cancers.
- Pathogenesis of paraneoplastic endocrine syndromes results from aberrant production by tumours of protein hormones, hormone precursors, or hormonelike substances.
- Cancers generally do not synthesize steroid hormones, except those arising in organs with physiological steroidogenesis (i.e., gonads or adrenals)
- Classifications schemes vary but most currently place PNS in one of five groups: endocrine, neurological, musculoskeletal, haematological, and other (e.g., skin)
- Cushing Syndrome is the Most common Paraneoplastic syndrome - associated with small cell Lung cancer

PNS Manifestation	Description / Mechanism	Commonly associated cancers
Cushing syndrome	Raised ACTH	Small cell lung CA
Hyponatremia (SIADH)	Raised ADH	Small cell lung CA
Hypercalcemia	Via PTHrp, abdominal pain, bone pain	Squamous cell Lung CA
Horner syndrome	Ipsilateral: Ptosis, miosis, anhidrosis	Apical lung CA
polycythaemia	↑ Erythropoietin (EPO)	RCC, HCC, hemangioblastoma
Acanthosis nigricans	velvety hyperpigmented plaques- axilla, neck	Obesity-Insulin resistance > GIT tumors
Sign of lesser treelet	Multiple seborrheic keratosis	GI cancers e.g., stomach CA
Myasthenia gravis	Antibodies against Ach receptors-at NMJ	Thymoma
Lambert- Eaton syndrome	Ab against pre-synaptic Ca ⁺ channels	Small cell lung CA
Opsoclonus myoclonus syndrome	Dancing eyes, dancing feet	Neuroblastoma (children)
NBTE (marantic endocarditis)	Deposition of sterile PLT thrombi on valves	GI Terminal neoplasm e.g., pancreatic CA
Pure red cell aplasia	Anaemia with low reticulocytes	Thymoma
Trousseau syndrome	Migratory superficial thrombophlebitis	Thymoma
Good syndrome	Hypogammaglobulinemia	Thymoma

Cachexia:

- Fat Loss + Muscle Wasting. TNF alpha play's main role in cachexia.
- IL- 1 & Proteolysis inducing factors also contribute to this syndrome.
- Cachexia is a devastating syndrome associated with the end-stage of several diseases, including cancer, and characterized by body weight loss and severe muscle and adipose tissue wasting.
- Although different cancer types are affected to diverse extents by cachexia, about 80% of all cancer patients experience this comorbidity, which highly reduces quality of life and response to therapy, and worsens prognosis, accounting for more than 25% of all cancer deaths.
- Cachexia represents an urgent medical need because, despite several molecular mechanisms have been identified, no effective therapy is currently available for this devastating syndrome.

P-Glycoproteins:

- ATP Dependant efflux pump contributing resistance to Anti-cancer drugs
- Multidrug resistant MDR1, more commonly referred to as P-gp or P-glycoprotein, is an efflux transporter that serves two major drug transport functions.
- Firstly, it restricts the distribution of its substrates into organs such as the brain, testes, placenta, and the GIT. Secondly, it expels drugs out of cells contributing to anti Neoplastic drug resistance

Autosomal dominant cancer syndromes	Autosomal recessive cancer syndromes
<ul style="list-style-type: none"> • Due to mutation of tumour suppressor genes • e.g., Familial adenomatous polyposis syndrome (FAP) • HNPCC, Rb gene mutations, Li – Fraumeni syndrome 	<ul style="list-style-type: none"> • Due to defective DNA Repair E.g., Xeroderma pigmentosa • Ataxia telangiectasia

SUMMARY & PAST PAPERS BCQS

1. Neoplasia is uncontrolled monoclonal proliferation.
2. A Cell must divide 30 times to reach 1 billion cells or 10^9
3. Moderate Dysplasia covers 2/3rd thickness of epithelium
4. Irreversible dysplasia that covers entire thickness of epithelium but doesn't cross it = Carcinoma in Situ
5. N/C ratio in cancer: 1: 1., normally it is 1:4 or 1: 6
6. Locally invasive tumors: BCC > Ameloblastoma
7. Most common cancer incidence in Males: Prostate > Lung > Colon
8. Cancer incidence in females: Breast > Lung > Colon
9. Highest Cancer related mortality in both sexes: Lung Cancer
10. Most common cancer in PAK: Lung Ca
11. Most common cancer in People of KARACHI: ORAL Cancer (betel nut – risk factor)
12. Cell – cell contact is lost by Inactivation of E – CADHERIN → Leads to Invasive cancer & Metastasis
13. Carcinoma spreads via Lymphatics & Sarcomas via Blood
14. Permeation is the spread of cancer cell in Lymphatics.
15. Special feature of Sarcomas: they have Inc Vascularity.
16. Diff b/ w Carcinoma & Sarcoma: Tissue of Origin > Increase Vascularity
17. Specific feature of Sarcoma = Inc Vascularity
18. Hematogenous spread is the most feared consequence of tumour
19. Spleen is least common site for metastasis and Lymph node is most common site followed by Liver & Lungs.
20. Four Carcinomas spread via Blood: HCC, RCC, Follicular thyroid carcinoma & Choriocarcinoma
21. Liver & Lungs are Most common sites of metastasis after Regional Lymph nodes
22. Regarding Endocrine glands, Adrenal glands are the most common site of metastasis
23. Lung cancer metastasizes commonly to Adrenal glands (if asking specifically about glands)
24. Metastasis to Brain: Lung > Breast > Melanoma > colon > Kidney
25. 50 % of brain tumors are metastatic and seen at grey- white junctions as well- circumscribed lesions
26. Metastasis to Colon: Liver > Stomach > Pancreas
27. Bone metastasis: Prostate > Breast > kidney > thyroid > Lung
28. Metastatic bone tumors are more common than primary tumors (Multiple Myeloma)
29. Lytic bone metastasis: Thyroid, Kidney, Non-small cell Lung Ca
30. Blastic lesions: Prostate, Small cell lung ca
31. Mixed lytic + Blastic lesions: Breast Cancer
32. Adenoma is benign tumour of epithelium
33. Anaplasia = Complete lack of differentiation of cell in tumour.
34. 75 – 100 % Undifferentiated or <25% differentiated cells in anaplasia.
35. Hamartomas are non-neoplastic disorganized masses in their native location e.g., Peutz jeghers polyps
36. Choriostoma = normal tissue in foreign Location e.g., Gastric tissue in distal ileum as in Meckel's diverticulum.
37. Grading is based on degree of cellular differentiation / nuclear differentiation & mitotic activity on histology
38. Staging is the degree of localization or spread based on site & size of primary lesion, **invasion, and metastasis.**
39. Staging is based on Clinical or pathological findings.
40. Stage determines Survival and has more Prognostic value
41. Metalloproteinases degrade basement membrane and ECM
42. KRAS Mutation: Colon & Pancreas cancer
43. BRCA mutation: Breast, ovary, pancreas Ca
44. Normal P53 activates P21 and blocks G1 → S phase
45. P53 mutations: Most cancers; Li - Fraumeni syndrome (Sarcoma, Breast Ca, Leukaemia, Adrenal tumour)
46. RB1 normally inhibits E2F, blocks G1 – S phase
47. RB1 mutation: Retinoblastoma & Osteosarcoma
48. In HNPCC: MLH – 1, MSH – 2 involved, DNA repair defect. Linked with Colorectal & Endometrial cancer
49. PTEN mutation: Prostate, Breast & Endometrial Ca
50. BCL – 2 mutations: Follicular & Diffuse large B cell Lymphoma
51. VHL gene inhibits Hypoxia inducible factor – 1, associated with Von- Hippau Lindau disease
52. Aflatoxins in stores grain & nuts may cause HCC
53. Azo dyes may cause Transitional Cell bladder Ca

54. Asbestos in shipyard workers, old roofing material causes: Bronchogenic Cancer > Mesothelioma
55. Ethanol may cause Squamous Cell cancer of Oesophagus
56. Radon: 2 nd common cause of Lung Ca after smoking
57. Non – Seminoma Testis germ cell tumour marker: AFP
58. Seminoma → Beta HCG, Most Radiosensitive Testicular tumour. Also secretes P- ALP
59. Lymphoma → LDH, Late age of presentation above 50 yrs., most radiosensitive tumour overall.
60. Embryonal Cell Carcinoma → AFP
61. Yolk sac Tumour → AFP > beta HCG, early presentation less than 4 yrs. of age. (children)
62. Choriocarcinoma → Beta HCG; Teratoma → All three Germ layers, Beta HCG and AFP
63. Granulosa Cell Tumour → Oestrogen; Sertoli Cell Tumour → Androgens
64. Dysgerminoma is counterpart of Seminoma
65. Most common Malignant Germ Cell Tumour is Dysgerminoma in female and Seminoma in male
66. ALP raised in Bone tumour, Pancreas, Seminoma
67. AFP marker of = Hepatoma & Yolk sac tumour
68. B HCG = marker for Choriocarcinoma
69. CA15-3/CA 27-29=Breast ca; Ca 19-9=Pancreas; Ca125=Ovary Ca
70. Calcitonin for Medullary thyroid Cancer
71. CEA=Colon cancer; PSA=Prostate cancer
72. S 100=Melanoma
73. Carcinoid tumour doesn't secrete hormonal tumour marker (as it is Neurotransmitter)
74. LDH: indicator of tumour burden
75. Definitive diagnosis of tumour: via Biopsy
76. For HCC: diagnostic is Triphasic CT – Scan
77. PSA is marker of recurrence after treatment.
78. Acid phosphatase is NOT a tumour marker (For Prostate it is Prostate specific acid – phosphatase)
79. Muscle tumors → Desmin
80. Epithelial tumors → Cytokeratin
81. Mesenchymal tumors → Vimentin, also RCC, Meningioma & endometrial Ca
82. Psammoma bodies in: Meningioma, Papillary thyroid cancer, Mesothelioma, Ovarian serous Cancer, Prolactinoma.
83. Cachexia: TNF – Alpha plays key role. Fat Loss + Muscle wasting
84. Lambert Eaton myasthenic syndrome: antibodies against Presynaptic Ca + channels
85. Myasthenia gravis: Ab against post synaptic Ach – receptors, present in Thymoma
86. Polycythaemia seen in: RCC, HCC, hemangioblastoma
87. Hypercalcemia: Squamous cell Lung ca, via PTH – rp.
88. Cushing syndrome + SIADH: in small cell Lung Ca
89. CD 10 +: marker of ALL
90. Microscopic feature for diagnosing tumour: Metastasis > Invasion > pleomorphism > increased N/C
91. For Pre-malignant Lesion: Pleomorphism is Diagnostic
92. Pre-malignant condition = Increased N/C ratio Diagnostic
93. Most Common Pre-malignant lesion – Leukoplakia
94. Most Lethal Pre-Malignant Lesion Erythroplakia
95. Most Common Pre-Malignant Condition- Submucosal Fibrosis
96. Most Lethal Pre-Malignant Condition – Lichen Planus
97. Most common skin Cancer: BCC – nodular type
98. Most common site of BCC: Upper lip
99. Most common site of SCC: Lower lip
100. Overall common cause of SCC: Bowen Disease > Actinic Keratosis
101. Lesion on Cheeks which needs excision: Actinic Keratosis
102. Blue cell tumour in children+ releasing catecholamine + gene Amplification = Neuroblastoma
103. Most Aggressive Cancer: Melanoma
104. Most Common Naevus in Children -Junctional nevus
105. Most Common Naevus in Adult is – Intradermal
106. Highest Malignant Potential- - Dysplastic Naevus
107. Angiosarcoma in Plastic Factory Worker – Vinyl chloride

108. Angiosarcoma in Farmer: Arsenic
109. Plastic factory worker: Liver Angiosarcoma
110. H/o Plastic Factory worker + Smoking: Lung Ca > Angiosarcoma
111. Hydrocarbon (Tyre Factory) + Aromatic Amines: Bladder CA
112. Smoke of tobacco is the most common carcinogen worldwide
113. Most common food source of carcinogen: Nitrosamines in Smoked Food (oesophageal & Gastric Cancer)
114. Smoking + Hydrocarbon – Lung CA > Bladder Cancer
115. Liver Cancer: -Alcohol > Aflatoxin > Smoking
116. Transitional Bladder CA- Smoking > Amines > Hydrocarbon
117. Squamous Cell Bladder CA- Schistosoma > Stones > Indwelling Catheter
118. Common method to detect Tumour – Tumour marker
119. Common method to detect Tumour cells – Peripheral smear
120. After Transplant most Common Malignancy-Skin
121. After Transplant Common malignancy in 1 or 5 Year – Lymphoproliferative
122. After Transplant Common malignancy after 10-15 Years = Skin
123. Radiation cause malignancy after – 10 years
124. Virus cause malignancy by using Oncogenes > Alteration in Protooncogene > alter. In Protein synthesis
125. Radiation cause malignancy by: They Have Proto oncogene and By Producing Free radicals
126. APC, RB, P53, WT1 are Tumour suppressor genes
127. MYC, Kit, RET, RAS, HER/Neu, ABL are Protooncogenes
128. Familial cancer presents at early age e.g., Breast, Ovary,
129. P53 is on chromosome 17, most common gene involved in Mutation causing Cancers
130. Balanced translocations produce cancer via Over – expression of genes
131. Ionizing Radiations cause; Leukaemia > Thyroid Cancer
132. Strontium – 90: Osteosarcoma > Leukaemia
133. CLL – not associated with radiations
134. UV rays: Skin cancer.
135. Tumour involving Lymph vessels: Cystic Hygroma (In turner syndrome)
136. Diff b/ w benign tumour & Hypertrophy: Capsule
137. Diff b/ w Malignant tumour & Benign: Metastasis
138. Multiple Washing techniques are used in: IMMUNOHISTOCHEMISTRY > ELISA
139. Protooncogenes are normal genes controlling cell growth
140. Lichen Planus incidence: 1 – 10 %
141. Risk of Lichen Planus changing into Malignancy is: 10 – 15 %
142. Low fibre diet cause- Colon cancer
143. High fat diet cause Breast cancer
144. Silicon in earth crust- may cause Silicosis
145. Most radiosensitive cell of body Is lymphocyte
146. Most radiosensitive testicular tumour is Seminoma, while most radiosensitive ovarian tumor is dysgerminoma.
147. Most radiosensitive lung tumour is small cell carcinoma of the Lung
148. Most radiosensitive tumour of bone tumors are Multiple myeloma and Ewing sarcoma
149. Most radiosensitive malignant brain tumour is Medulloblastoma
150. Most radiosensitive renal tumour is Wilms tumour
151. Epithelial cells neoplasia is common with: Cytokeratin
152. Coin lesion on chest x ray of a woman, how to differ between granuloma and neoplasia: Rapid increase in size
153. Reversible abnormal shape size and loss of cellular orientation is -- Dysplasia
154. Women who have Leiomyoma and epithelium covering endometrium shows abundant stroma with a smaller number of endometrial glands, what's happening in Endometrium: Atrophy
155. Undescended testes are associated with which complication: Neoplasia > infertility
156. Which of the following is not carcinogen = Alcohol (indirect carcinogen)
157. Carcinoma is not related to = iodine deficiency
158. Which among following chemicals exposure causes carcinoma = Benzene
159. Which is carcinogen = alcohol for liver. Which is NOT chemical carcinogen → sodium methylsulfate.

GENETICS

Basic Concepts	<ul style="list-style-type: none"> In humans, the normal chromosome count is 46 (i.e., $2n = 46$) Any exact multiple of the haploid number (n) is called euploid. Chromosome numbers such as $3n$ and $4n$ are called polyploid. Polyploidy generally results in a spontaneous abortion. Any number that is not an exact multiple of n is called aneuploidy. The chief cause of aneuploidy is the non-disjunction of a homologous pair of chromosomes at 1st meiotic division or a failure of sister chromatids to separate during the second meiotic Division. Mosaicism is the presence of two or more populations of cells in the same Individual. Mutation means a permanent change in DNA. The most common form of DNA is B - DNA, which is a right-handed, helical DNA, with 10 base pairs Per turn. This is the form of DNA found in humans and most organisms. X Chromosome is submetacentric and Y chromosomes is Acrocentric type
Types of Chromosomes	<ol style="list-style-type: none"> Metacentric = 2 equal arms with chromatids in centre Submetacentric = Centromere is slightly away from centre e.g., X chromosome Acrocentric = Centromere is towards one end e.g., Y chromosomes Telocentric are Not seen in humans
Nucleotide	<ul style="list-style-type: none"> Composed of a Nitrogenous base, pentose sugar and a Phosphate group Nucleotide is formed Through Phosphorylation of nucleoside. A nucleotide is acidic in nature
Nucleoside	<ul style="list-style-type: none"> It is composed of only a Nitrogenous base + a phosphate Group. It is a component of the nucleotide and is slightly basic in nature
DNA	<ul style="list-style-type: none"> Exists in condensed chromatin form inside nucleus. B- DNA is the most common form in humans. Double stranded molecule, both strands run in Opposite directions. Uracil is absent. Sugar moiety is Deoxyribose and Bases are = adenine, guanine, cytosine and thymine It is the genetic and hereditary Material of cells. Hydrolysis of DNA gives Phosphoric acid. The Genetic disease mostly has Pathology in DNA DNA replications occur in interphase (S phase) 5'-3' direction in Okazaki fragments (continuous & discontinuous Fashion). Helicase unwinds DNA at replication fork – deficient in Bloom syndrome. Topo-isomerases creates breaks in DNA to add or remove supercoils. DNA Ligase catalyses formation of phosphodiester bond within a strand of double stranded DNA and Joins Okazaki fragments. Two Hydrogen bonds b/w adenine – Thymine, three Bonds b/w Guanine – Cytosine. Inc Guanine – Cytosine content (G- C Content): increase Melting Point of DNA Histone protein present in DNA. Lysine + Arginine gives histones +ve charge. Phosphates give -ve charge. Euchromatin is Transcriptionally active DNA, loosely coiled or less condensed, easily transcribed. Heterochromatin is Transcriptionally inactive DNA, tightly coiled and highly condensed that maintains structural integrity of genome. Histone Methylation makes DNA Mute (inactivates) and Acetylation activates DNA Introns are intervening non-coding segment of DNA-(97% of the human Genome) that do not code of proteins but regulate gene expression. Exons contain the actual genetic information coding for the protein (3% of the Human genome). (E for Exons & Expression) DNA – Polymerase – I: in prokaryotes only, degrades RNA primer to replace with DNA. It also excises RNA primer via 3'-5' exonuclease. DNA Polymerase- III in prokaryotes only, has 5'-3' synthesis and proofreading with 3'→5' exonuclease.

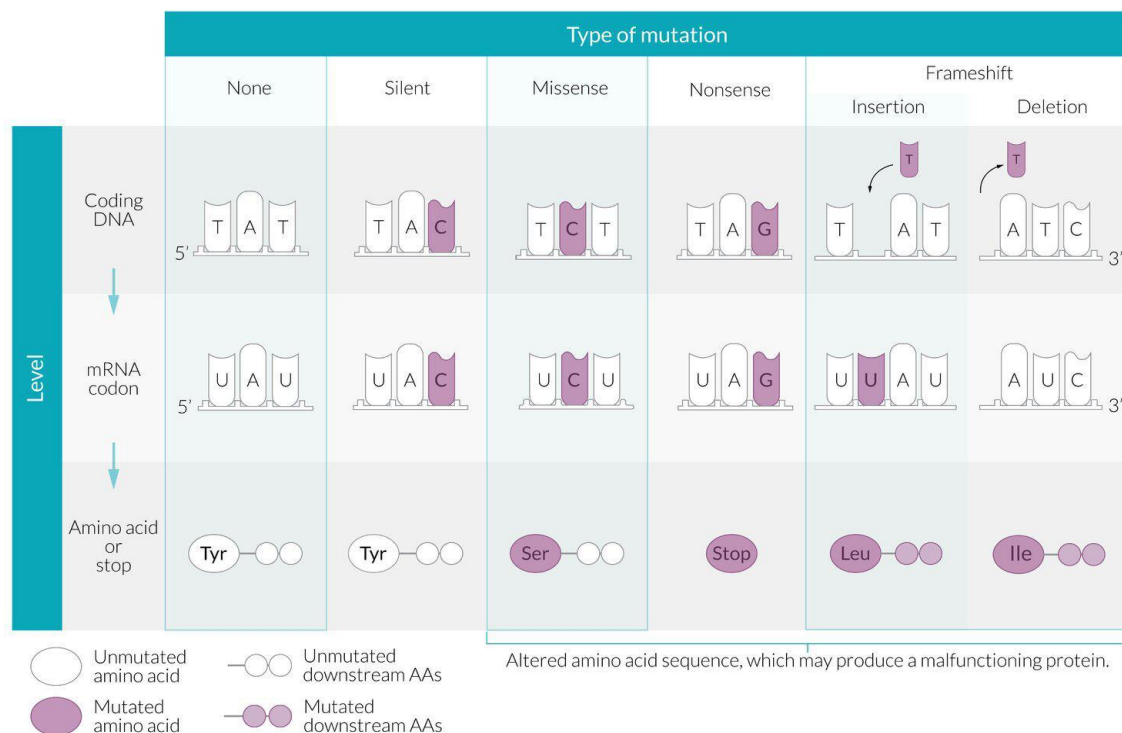
	<ul style="list-style-type: none"> • Telomerase: A reverse transcriptase (RNA dependant DNA polymerase) adds DNA to 3' end to avoid loss of genetic material. Tumors achieve limitless replicative potential via Telomerase activity. • Decreased Telomerase activity is linked to aging.
DNA Repair	<p><u>Double stranded repair:</u></p> <ol style="list-style-type: none"> 1. Non – Homologous end joining Brings together 2 ends of DNA fragments to repair double stranded breaks. Some DNA may be lost. It is defective in Ataxia telangiectasia. 2. Homologous Recombination: A strand from damaged dsDNA is repaired using complementary strand from intact homologous ds DNA as a template.it requires 2 homologous DNA complexes. <p><u>Single stranded repair:</u> via NER, BER, MMR as given below:</p> <ol style="list-style-type: none"> 1. Nucleotide excision repair occurs in G1 phase. Repairs bulky lesions via endonucleases that release oligonucleotides containing damaged bases, DNA polymerase + Ligase fill and seal the gap respectively. NER is Defective in Xeroderma Pigmentosa (inability to repair DNA Pyrimidine dimers caused by UV-Light) 2. Base excision repair occurs throughout cell cycle. Imp in repairing toxic or spontaneous deamination. 3. Mismatch repair occurs mainly in S phase. MMR is defective in LYNCH Syndrome (hereditary nonpolyposis colorectal cancer HNPCC)

MUTATION

Permanent change in DNA caused by Various factors. Types are explained below.

Basis of Classification	Major type of mutation & Features
Origin	<ul style="list-style-type: none"> • Spontaneous mutation occurs in the absence of unknown mutagen. • Induced mutation occurs in the presence of known mutagen
Cell type	<ul style="list-style-type: none"> • Somatic mutation occurs in non-reproductive cells. • Germ line occurs in reproductive cells
Effect on function	<ul style="list-style-type: none"> • Loss of function or null mutation eliminates normal function. • Hypomorphy or leaky reduces normal function. • Hypermorphic increases normal function. • Gain of Function mutation: expressed at incorrect time or inappropriate cells
Molecular change (Nucleotide substitution)	<ul style="list-style-type: none"> • Transition: a base pair in DNA duplex is replaced with a different base pair e.g., Purine to purine (A → G); Pyrimidine to pyrimidine (T → C) • Transversion: purine to pyrimidine (A → T); pyrimidine to purine (C → G) • Insertion: 1 or more extra nucleotide present • Deletion: 1 or more nucleotide is missing
Effect on translocation (Gene mutations)	<ol style="list-style-type: none"> 1. Point Mutations: Silent, Missense, Non-Sense 2. Frame shift Mutations: Addition (insertion) or deletion 3. Splice site mutations: due to Retained intron in mRNA e.g., in Marfan syndrome. <ul style="list-style-type: none"> • Silent or synonymous mutation: no change in amino acid encoded. • Missense mutation/non-synonymous: change in amino acid encoded e.g., sickle cell anaemia. • Non-sense: creates stop codon e.g., UGA, UAA, UAG', occurs in thalassemia. • Frame shift mutation: shifts triplets reading of codon out of correct phase. caused by insertions or deletions of several nucleotides in a DNA sequence that is not divisible by three. Protein may be shorter or longer with altered function. Examples: Duchenne muscular dystrophy & Tay sach's disease
Chromosomal mutations	<p>They may be Numerical or Structural</p> <ol style="list-style-type: none"> 1. Numerical: Aneuploidy (abnormal no. of chromosome) may be; monosomy i.e., one missing chromosome (Turner syndrome) Trisomy i.e., extra chromosome (Down's syndrome) or Tetrasomy as well 2. Structural: 4 types → Deletion, duplication, inversion and translocation

	Deletion	<ul style="list-style-type: none"> it occurs when nucleotides are left out of gene and usually cause a shift in reading frame that will ultimately truncate the protein. can be caused by errors in chromosomal crossover in meiosis
	Duplication	<ul style="list-style-type: none"> portion of chromosome duplicates resulting in extra genetic material Arise from an event termed unequal crossing-over that occurs during meiosis between misaligned homologous chromosomes.
	Inversion	<ul style="list-style-type: none"> A portion of the chromosome has broken off, turned upside down, and reattached, therefore the genetic material is inverted
	Translocation	<ul style="list-style-type: none"> Reciprocal translocation caused by rearrangement of parts between nonhomologous chromosomes. If no genetic material is lost during the exchange, the translocation is a balanced translocation



POLYMORPHISM

- DNA sequence variation between 2 individuals is known as polymorphism and it is 0.5 % approx.
- As the 2 individuals share > 99.5 % of DNA sequence

Types of Polymorphism:

- Single Nucleotide Polymorphism** - SNP: Most common type, more than 6 million SNP.
- Single nucleotide / 1000 base pairs. Present in both exons & Introns. Less than 1% in coding regions
- Copy Number Variations** – CNV: consisting of different no. Of large contiguous stretches of DNA from 1000 to Million base pairs. CNVs form basis of phenotypic diversity. 50 % of coding regions.
- Repeat Length Polymorphism**: Short repetitive sequence of DNA Variation. May be Microsatellite or Minisatellite
 - Microsatellite: 2 – 6 base pairs repeat size, < 1 kilobase
 - Minisatellite: 15 – 70 base pairs repeat size, 1 – 3 kilobase.

RNA (RIBONUCLEIC ACID)

- RNA is Single strand molecule involved in the synthesis of Protein i.e., translation.
- Thymine base is absent while sugar moiety is ribose in RNA.

Types of RNA	Types of RNA: <ol style="list-style-type: none"> 1. mRNA is the longest type (m for massive): Capping (7- Methylguanosine cap) + polyadenylation + Splicing out of introns occurs. Hence, Capped, Tailed, and spliced transcript = m RNA. 2. t RNA- the smallest type (t for tiny) 3. rRNA - the most abundant type (r for rich or abundant)
Translation	Correct sequence of protein synthesis or Translation = (MC – RTA) 1. mRNA → 2. cytoplasm → 3. ribosome → 4. tRNA → 5. amino acid
Post-translational modifications	<ol style="list-style-type: none"> 1. Trimming: Removal of N or C – terminal peptides from zymogen to generate mature protein e.g., trypsinogen- trypsin. 2. Covalent Alteration: methylation, acetylation, hydroxylation, glycosylation, phosphorylation & Ubiquitination. 3. Chaperones Protein: Facilitate and maintain protein folding to prevent protein misfolding
Non-functional RNAs	<ol style="list-style-type: none"> 1. Micro RNA (miRNA; 22 nucleotides): <ul style="list-style-type: none"> • They do not encode proteins due to Post transcriptional gene silencing. • Inhibit gene expression by blocking mRNA Induced translation via RISC (RNA induced Silencing complex) 2. SiRNA (Exogenous miRNA): Useful laboratory tool to study gene function and therapeutic agents by knock down technology. 3. Long Non-Coding RNA: > 200 nucleotides, promote gene activation while inhibit gene transcription.

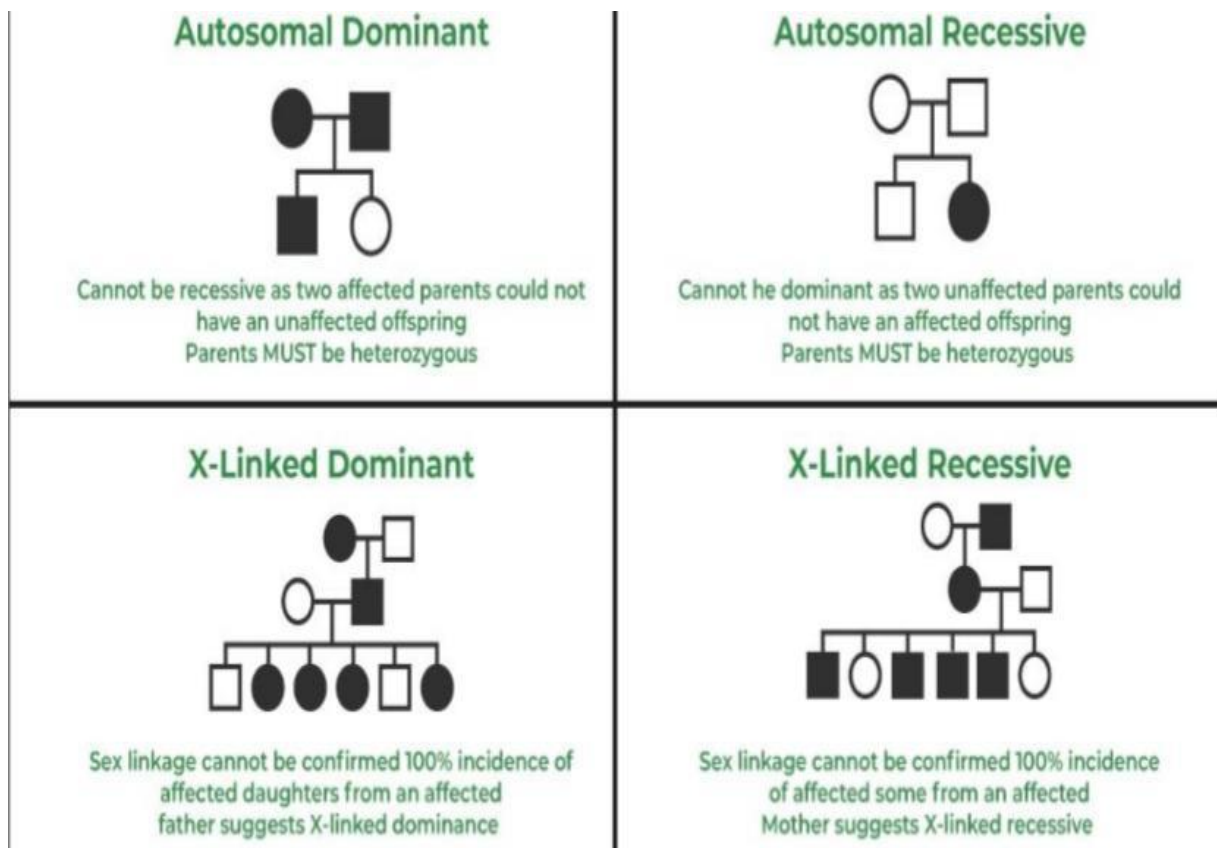
Genetic Term	Description
Gene	<ul style="list-style-type: none"> • The basic physical and functional unit of hereditary information which are made up of DNA. • Act as instructions to make molecules called proteins. • In humans, genes vary in size from a few hundred DNA bases to more than 2 million Bases. • There are 30,000 essential genes which cause the formation of 30,000 types of protein. • Genes (DNA molecules) control the formation of mRNA which control the Formation of proteins
Genome	<ul style="list-style-type: none"> • A genome is all the genetic material (DNA) in the chromosome of a particular organism. • its size generally given as its total number of base pairs
Genetic code	<ul style="list-style-type: none"> • Features: Universal, comma less, non-Overlapping, degenerate or redundant & Unambiguous • Degenerate or redundant means most amino acids are coded by multiple codons. • Wobble Hypothesis: codons that differ in 3rd position may code for same tRNA or amino acid. • Start codons AUG codes for methionine in eukaryotes and N- Formyl methionine in Prokaryotes. • Stop Codons: UGA (U go away), UAA (U are away), UAG (U are gone)
Genotype	<ul style="list-style-type: none"> • It is the genetic makeup of an organism or individual e.g., genes for eye and hair colour
Phenotype	<ul style="list-style-type: none"> • Detectable expression of the genotype, an expressed and observable trait that isn't inherited. Phenotype is the physical appearance of that trait e.g., hair colour, eye colour and weight. • Phenotypic sex refers to an individual's sex as determined by their internal & external genitalia, expression of secondary sex characteristics and behaviour.
Codominance	Both alleles contribute to the phenotype of the heterozygote. Example of blood Group A, B & AB

Complete penetrance	The allele is said to have complete penetrance if all individuals who have the disease causing-mutation have clinical symptoms of the disease				
Incomplete penetrance	Not all individuals with a mutual genotype show the mutant phenotypic effects. Example: BRCA1 gene mutations don't always result in the breast or ovarian cancer				
Variable expressibility	Phenotype varies among individuals with the same genotype. Example: two Patient with neurofibromatosis type I may have varying disease severity				
Mosaicism	Presence of genetically distinct cell lines in the same individuals <ol style="list-style-type: none"> Somatic mosaicism: mutation arises from post fertilization meiotic errors Genetic mosaicism: mutation in only egg or sperm <ul style="list-style-type: none"> if parents and relatives of patient don't have the disease → suspect germline or gonadal mosaicism 				
Pleiotropy	<ul style="list-style-type: none"> One gene contributes to multiple phenotypic effects. Example: PKU causes many symptoms ranging from mental retardation to hair/skin changes 				
Twin study	An experiment that asses genetic and environmental influence on a trait using MZ and MD twin pairs				
Heteroplasmy	Mitochondrial DNA (Mt DNA) passes from mother to all children. Presence of both normal and mutated Mt DNA resulting in variable expression in mitochondrially inherited diseases.				
Uniparental-disomy	In this case, Offspring receives 2 copies of chromosome from 1 parent and no copy from other parent. <ol style="list-style-type: none"> Heterodisomy: Heterozygotes indicate Meiosis I error Isodisomy: Homozygotes indicate Meiosis II error 				
Anticipation	Increase severity and earlier onset of a disease in successive generations e.g., Huntington's chorea.				
Epigenetic changes	Modulation of gene or protein expression in the absence of alterations in DNA sequence (mutation) or structure of the encoding gene. Useful in regulation of: <ul style="list-style-type: none"> Tissue specific gene expression Genomic imprinting: 1 copy is silenced by Methylation and other is expressed i.e., parent of origin effects. X chromosome inactivation and Fragile x syndrome 				
Genomic Imprinting	<ul style="list-style-type: none"> Epigenetic process resulting in differential inactivation of Maternal/paternal alleles of certain Genes. Heritable chemical modification → Methylation of DNA or acetylation of Histones Decreases genetic expression (without affecting primary DNA sequence → epigenetics) Occurs in sperm or ova before Fertilization. Maternal genomic imprinting: Selective inactivation of maternal allele e.g., Angelman syndrome Paternal genomic imprinting: Selective inactivation of paternal allele e.g., Prader-Willi syndrome. <table border="1"> <tr> <td>Prader-Willi syndrome</td><td> <ul style="list-style-type: none"> Maternally derived genes are silenced, chromosome 15 of paternal origin involved. Disease occurs when the paternal allele is deleted or mutated. Presents with Hyperphagia, obesity, intellectual disability, Hypogonadism, Hypotonia. 25% of cases are due to maternal uniparental Disomy </td></tr> <tr> <td>Angelman syndrome</td><td> <ul style="list-style-type: none"> Paternally derived UBE3A is silenced. Disease occurs when the maternal allele is deleted or mutated. Presents with: Seizures, Ataxia, Intellectual disability and inappropriate Laughter. UBE3A on maternal copy of chromosome 15 is involved in the disease process. 5 % of cases are due to paternal uniparental disomy. </td></tr> </table>	Prader-Willi syndrome	<ul style="list-style-type: none"> Maternally derived genes are silenced, chromosome 15 of paternal origin involved. Disease occurs when the paternal allele is deleted or mutated. Presents with Hyperphagia, obesity, intellectual disability, Hypogonadism, Hypotonia. 25% of cases are due to maternal uniparental Disomy 	Angelman syndrome	<ul style="list-style-type: none"> Paternally derived UBE3A is silenced. Disease occurs when the maternal allele is deleted or mutated. Presents with: Seizures, Ataxia, Intellectual disability and inappropriate Laughter. UBE3A on maternal copy of chromosome 15 is involved in the disease process. 5 % of cases are due to paternal uniparental disomy.
Prader-Willi syndrome	<ul style="list-style-type: none"> Maternally derived genes are silenced, chromosome 15 of paternal origin involved. Disease occurs when the paternal allele is deleted or mutated. Presents with Hyperphagia, obesity, intellectual disability, Hypogonadism, Hypotonia. 25% of cases are due to maternal uniparental Disomy 				
Angelman syndrome	<ul style="list-style-type: none"> Paternally derived UBE3A is silenced. Disease occurs when the maternal allele is deleted or mutated. Presents with: Seizures, Ataxia, Intellectual disability and inappropriate Laughter. UBE3A on maternal copy of chromosome 15 is involved in the disease process. 5 % of cases are due to paternal uniparental disomy. 				

Single gene disorders	Classical Mendelian inheritance	Autosomal disorders: autosomal dominant (AD) and autosomal recessive (AR) X linked disorders: X linked dominant (XD) and X linked recessive
	Non-Mendelian inheritance	Mitochondrial inheritance, genomic imprinting, germ line mosaicism and Trinucleotide repeat mutations (extensions)
Multifactorial inheritance	Complex Polygenic inheritance. 2 or more genes and environmental factors are involved. Examples: DM, HTN, IHD, Gout, Cleft Lip & Cleft Palate etc. Overall, it is the most common pattern of inheritance	

Autosomal recessive inheritance	<ul style="list-style-type: none"> AR disorders are the most common Mendelian disorders (also the largest group) All siblings have a chance of one into four of contracting this disease (1: 4) Mostly are enzyme deficiency disorders or metabolic diseases. They occur when both alleles at a given gene locus are mutants. The trait does not usually affect the parents, but siblings may show the disease. Siblings have one chance in four of being affected (i.e., the recurrence risk is 25% for each Birth) If the mutant gene occurs with a low frequency in the population, there is a strong Likelihood that the Proband (the first affected family member) is the product of a consanguineous marriage. <p>Examples:</p> <ul style="list-style-type: none"> Hemochromatosis is the most common AR disease. Thalassemia and sickle cell disease, Glycogen Storage disease, Alpha-1 antitrypsin deficiency Autosomal Recessive polycystic kidney disease: (ARPKD)—infantile PKD Cystic fibrosis, Wilson disease, Congenital adrenal hyperplasia Note: most of AR diseases are enzymes deficiencies or metabolic disorders causing early death
Autosomal dominant inheritance	<ul style="list-style-type: none"> Often due to defect in Structural genes and pleiotropic, hence, family history crucial to diagnosis The child can be affected if only one of the parents affected. Autosomal dominant disorders are manifested in the heterozygous state; at least one parent of an index case is usually affected; both males and females are affected, and both can transmit the Condition. When an affected person marries an unaffected one, every child has one chance in two of having the disease. <p>Examples:</p> <ul style="list-style-type: none"> Von Willebrand disorder - most common AD disorder Achondroplasia-the failure of longitudinal bone growth (enchondral ossification) Short limbs (caused by a gain in function mutation in the FGFR3 gene located on the Short Arm of Chromosome 4, which affects enchondral bone formation) Retinoblastoma, Hereditary spherocytosis Autosomal Dominant Adult polycystic disease (ADPKD), Osteogenesis imperfecta, Neurofibromatosis Pseudohypoparathyroidism, Familial polyposis coli, Myotonic dystrophy Marfan syndrome, Acute intermittent porphyria, Familial Hypercholesterolemia
X linked recessive inheritance	<ul style="list-style-type: none"> Males are commonly more affected than female. It may skip generations. Most X-linked disorders are X-linked recessive. All sex-linked disorders are X-linked. No Y-linked diseases are yet known. On the Y chromosome is the attribute of hairy ears XR disorders are transferred from a female carrier to sons only An affected male does Not transmit the disorder to sons, but all daughters are carriers Sons of Women have one chance in two of receiving the mutant gene.

	<p>Examples:</p> <ul style="list-style-type: none"> Haemophilia A, B, Duchene muscular dystrophy, G6PD deficiency, Wiskot- Aldrich Syndrome, Bruton's disease. 						
X linked dominant inheritance	<p>it is a mode of genetic inheritance by which dominant gene is carried on the X chromosome.</p> <p>it is less common than the X-linked recessive type and affects the females more</p> <p>Example: Rett syndrome, Alport syndrome, Hypophosphatemia rickets.</p>						
% of offspring affected	<table> <tr> <td>AD</td><td>50% affected children if 1 parent is heterozygote and other is unaffected. 75 % offspring affected if 2 heterozygotes affected parents. 100% offspring affected if 1 homozygous affected (diseased) parent.</td></tr> <tr> <td>AR</td><td>0 % children affected if 1 carrier parent and 1 homozygous unaffected parent. 25% children affected if 2 heterozygote carrier parents. 50% children affected if 1 homozygous affected parent and 1 heterozygous carrier parent.</td></tr> <tr> <td>XR</td><td>50% sons affected if mother is carrier while 100 % sons affected if mother is diseased.</td></tr> </table>	AD	50% affected children if 1 parent is heterozygote and other is unaffected. 75 % offspring affected if 2 heterozygotes affected parents. 100% offspring affected if 1 homozygous affected (diseased) parent.	AR	0 % children affected if 1 carrier parent and 1 homozygous unaffected parent. 25% children affected if 2 heterozygote carrier parents. 50% children affected if 1 homozygous affected parent and 1 heterozygous carrier parent.	XR	50% sons affected if mother is carrier while 100 % sons affected if mother is diseased.
AD	50% affected children if 1 parent is heterozygote and other is unaffected. 75 % offspring affected if 2 heterozygotes affected parents. 100% offspring affected if 1 homozygous affected (diseased) parent.						
AR	0 % children affected if 1 carrier parent and 1 homozygous unaffected parent. 25% children affected if 2 heterozygote carrier parents. 50% children affected if 1 homozygous affected parent and 1 heterozygous carrier parent.						
XR	50% sons affected if mother is carrier while 100 % sons affected if mother is diseased.						
Key Facts	<ul style="list-style-type: none"> Males are affected more in XR diseases. No male is affected if father has the disease or affected. In XR pattern, Sons get allele from mother while daughter from either parent Male and female equally affected in AD, AR and mitochondrial pattern Only the recessive diseases (AR, XR) can be inherited from Unaffected parents 						



AUTOSOMAL TRISOMIES

Down's Syndrome, Edwards Syndrome, Patau syndrome are the autosomal Trisomies.
Autosomal monosomies are incompatible with life.

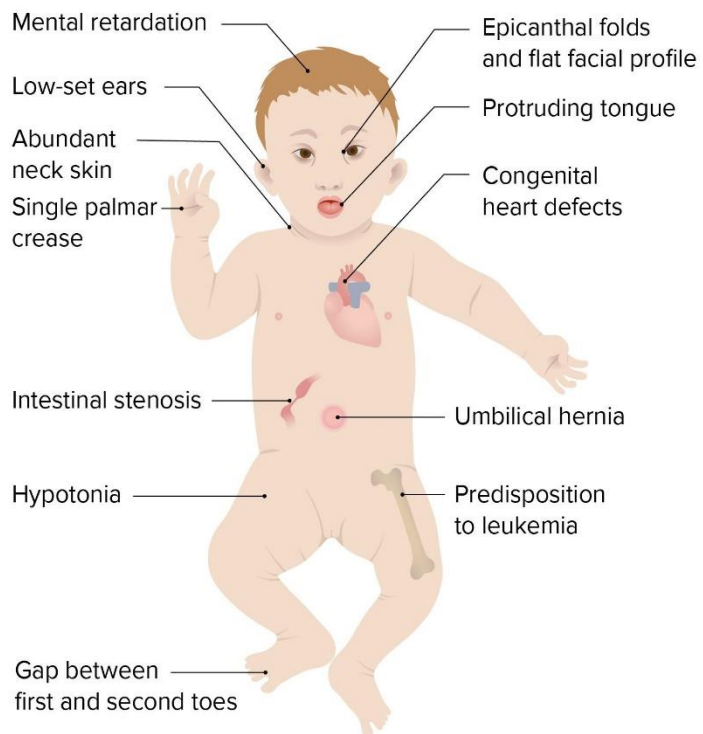
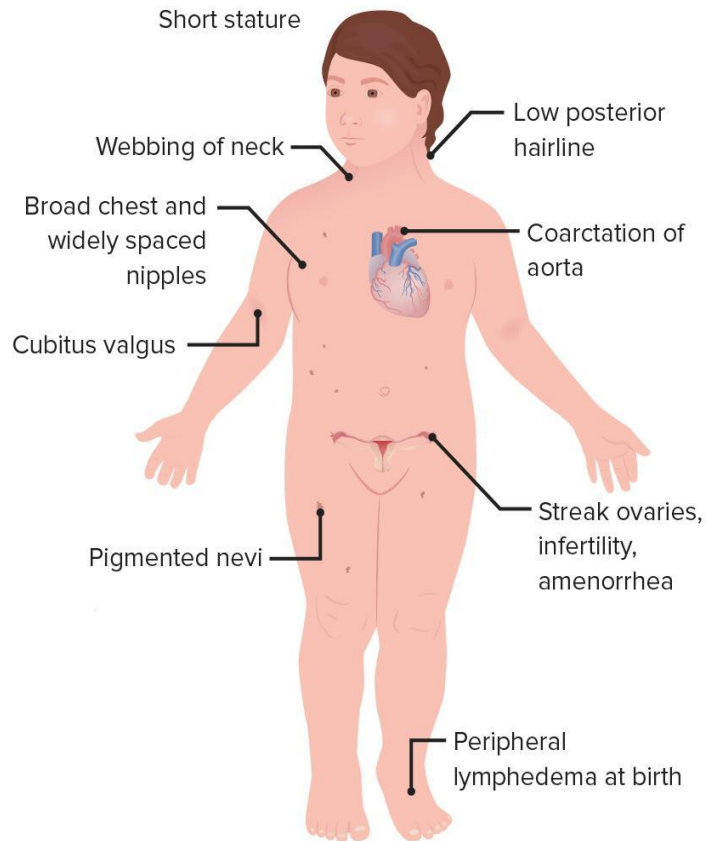
<p>Down's syndrome (Trisomy 21)</p>	<ul style="list-style-type: none"> ❖ 95% of affected persons have trisomy 21, so their chromosome count is 47 or (47XY) three 21st ❖ Down syndrome is the most common chromosomal disorder. ❖ in 95% of cases, the extra chromosome is of maternal origin. ❖ Incidence: 1: 700. Incidence increases with maternal age. 10 folds risk increases every 10 years. • Mother's age < 20 yrs. incidence of down syndrome is 1:1500. 30 yrs.: 1:1000, 35 yrs.: 1:35, 40 yrs.: 1:10, > 45 yrs. 1: 25 while at 50 yrs. it is 1:10 • The parents of such children have a normal karyotype and are normal in all respects. <p><u>Associations of Down syndrome:</u></p> <ul style="list-style-type: none"> ❖ Non-disjunction 90 % ❖ Robertsonian translocation 4% ❖ Mosaicism 1% ❖ Associated with ASD, AML > ALL, hypothyroidism and duodenal atresia (double bubble sign on X-ray) ❖ Increase risk of Alzheimer disease at 35 yrs. of age ❖ Endocardial cushion defects are most common CVS related defects in this. ❖ Advanced maternal age is a risk factor. <p><u>Risk of Down Syndrome:</u></p> <ul style="list-style-type: none"> ❖ If mother is carrier of Trisomy 21, risk of DS in baby is 100% ❖ If father is a carrier the risk in baby is 5 % ❖ Robertsonian translocation's transmission in next generation: 33 % (1/3) ❖ Risk of Down syndrome in next baby if mother having Robertsonian translocation: 15% (5% is given often in options so choose 5% over there) <p><u>Clinical features</u></p> <ul style="list-style-type: none"> • Characteristic clinical features of Down syndrome include epicanthic folds and flat facial Profile • Protruding tongue and umbilical hernia are typical clinical features • Simian Crease – single Palmar crease, Bursh field spots in iris, Hirschsprung's disease • Trisomy 21 is the most common genetic cause of mental retardation. • The degree of Mental retardation is so severe that IQ varies from 25 to 50 • Increased Nuchal Translucency and hypoplastic nasal bone • Congenital malformations are common and quite disabling. • Approximately 40% of patients with trisomy 21 have cardiac malformations, which are Responsible for most of the deaths in early childhood. • Serious infections are another important cause of morbidity and mortality. <p><u>Screening Tests:</u></p> <ul style="list-style-type: none"> ❖ To early detect malformations - USG is preferred. ❖ Quadruple tests: High levels of HCG & Inhibin while Low levels of AFP & Estriol
<p>Edward syndrome (Trisomy 18)</p>	<ul style="list-style-type: none"> ❖ Incidence 1:8000. Election age (18). ❖ 2nd most common autosomal trisomy resulting in live birth (most common is Down syndrome). ❖ In Edwards syndrome, every prenatal screening Marker decreases. <p><u>Findings: Mnemonics - PRINCE Edward</u></p> <ul style="list-style-type: none"> ❖ Prominent occiput ❖ Rocker-bottom feet ❖ Intellectual disability ❖ Nondisjunction ❖ Clenched fists with overlapping fingers ❖ low-set Ears ❖ micrognathia (small jaw) ❖ congenital heart disease, ❖ omphalocele, myelomeningocele, Spina bifida, myelomeningocele ❖ Death usually occurs by age 1

Patau syndrome (Trisomy 13)	<ul style="list-style-type: none"> ❖ Incidence 1:15,000, Puberty at age 13. ❖ Defect in fusion of prechordal mesoderm causes Midline defects. <p>Findings:</p> <ul style="list-style-type: none"> ❖ severe intellectual disability ❖ rocker- Bottom feet ❖ microphthalmia, microcephaly ❖ Cleft lip/palate, holoprosencephaly, Polydactyly ❖ cutis aplasia, congenital heart (pump) disease, polycystic kidney disease and Omphalocele. ❖ Death usually occurs by age 1.
---------------------------------------	---

Remember:

- Horseshoe kidneys in turner syndrome but polycystic kidneys in Patau's syndrome (p for polycystic & Patau)
- Spina bifida linked with Edward syndrome.

Turner syndrome (45XO)	<ul style="list-style-type: none"> • (45 XO) • Also known as complete or permanent Monosomy X • Mosaicism is the most common cause of turner syndrome. • Incidence of TS is 1: 3000. • The most common cause of primary amenorrhea in women is TS • Turner syndrome, characterized by primary hypogonadism in phenotypic females, results from Partial or complete monosomy of the short arm of the X chromosome. • Diagnosis is established by karyotyping for chromosomal analysis. • Karyotype 45XO – Confirmatory test • Scanty bar body or No body is present in TS – screening test. <p>Clinical features:</p> <ul style="list-style-type: none"> • Combination of Short stature and primary amenorrhea should prompt Strong suspicion of TS. • Webbed neck-caused by dilated lymphatic channels (cystic hygroma) and streak ovaries. • Associated with preductal Coarctation, bicuspid aortic valve, Horseshoes kidney, hypothyroidism. • Risk of Ovarian dysgerminoma is also there
Klinefelter's syndrome (47XXY)	<ul style="list-style-type: none"> • 47XXY/47XXX with \uparrow FSH, LH & Oestrogen but \downarrow Testosterone & Inhibin • Most common sex chromosomal abnormality is KS • Male hypogonadism that develops when there are at least two X Chromosomes and one or more Y-chromosomes. Most patients are 47, XXY. • This karyotype results from the non-disjunction of sex chromosomes during meiosis. • The extra X chromosome may be of either maternal or paternal origin • Advanced maternal age and a history of irradiation of either parent may contribute to the meiotic error resulting in this condition. <p>Clinical features:</p> <ul style="list-style-type: none"> • Tall statures and Small firm testes are typical • Reduced facial, body and pubic hair & Gynecomastia are also frequently noted. • Along with the testicular atrophy, the serum testosterone levels are lower than normal but urinary Gonadotropin levels are elevated. • KS is the most common cause of hypogonadism in males • Dysgenesis of seminiferous tubules and abnormal Leydig cell function • KS may be present in 3 to 7 % of men with breast cancer



Cri – du chat Syndrome

- Cri du chat = cry of the cat. Congenital deletion on short arm of chromosome 5 (46, XX or XY, 5p-).
- **Findings:** microcephaly, intellectual disability, high-pitched cry, epicanthal Folds & cardiac abnormalities (VSD).

William' s Syndrome:

- Congenital microdeletion of long arm of chromosome 7
- Findings: distinctive “elfin” facies, intellectual disability, hypercalcemia, verbal Skills, extreme friendliness with strangers, cardiovascular problems (e.g., supravulvar aortic Stenosis, renal artery stenosis)

True hermaphrodite	<ul style="list-style-type: none"> • XX > XX/XY > XXY • True hermaphrodites have ovaries and testes in same individual- also called Ovotestes. 				
Pseudo-hermaphrodite	<p>An individual having gonad of only one sex (either ovary or testis) but external Genitalia and secondary characters of opposite sex.</p> <table> <tr> <td>Male pseudohermaphrodite</td><td> <p>An individual having Testes but phenotypically resembles to female. Genotype: 46XY Causes:</p> <ul style="list-style-type: none"> • Testicular feminization syndrome – most common cause • Hormones administered to mother during pregnancy. • Defects in testosterone synthesis </td></tr> <tr> <td>Female pseudohermaphrodite</td><td> <p>Masculinized female having Ovaries but phenotypical male. Genotype: 46XX Causes:</p> <ul style="list-style-type: none"> • Congenital adrenal hyperplasia or Adrenogenital syndrome-most common cause • Adrenal or Ovarian tumour secreting androgen • hormones administered to mother in pregnancy </td></tr> </table>	Male pseudohermaphrodite	<p>An individual having Testes but phenotypically resembles to female. Genotype: 46XY Causes:</p> <ul style="list-style-type: none"> • Testicular feminization syndrome – most common cause • Hormones administered to mother during pregnancy. • Defects in testosterone synthesis 	Female pseudohermaphrodite	<p>Masculinized female having Ovaries but phenotypical male. Genotype: 46XX Causes:</p> <ul style="list-style-type: none"> • Congenital adrenal hyperplasia or Adrenogenital syndrome-most common cause • Adrenal or Ovarian tumour secreting androgen • hormones administered to mother in pregnancy
Male pseudohermaphrodite	<p>An individual having Testes but phenotypically resembles to female. Genotype: 46XY Causes:</p> <ul style="list-style-type: none"> • Testicular feminization syndrome – most common cause • Hormones administered to mother during pregnancy. • Defects in testosterone synthesis 				
Female pseudohermaphrodite	<p>Masculinized female having Ovaries but phenotypical male. Genotype: 46XX Causes:</p> <ul style="list-style-type: none"> • Congenital adrenal hyperplasia or Adrenogenital syndrome-most common cause • Adrenal or Ovarian tumour secreting androgen • hormones administered to mother in pregnancy 				
Congenital adrenal hyperplasia (46 XX) Or Adrenogenital syndrome	<ul style="list-style-type: none"> • CAH or adrenogenital syndrome is the most common cause of Female Pseudohermaphrodites (46 XX) • Most common enzyme deficiencies are: 21 alpha hydroxylase > 17 hydroxylase > 11 hydroxylases. • In Females symptoms are Masculinization/Virilization, ambiguous genitalia, enlarged clitoris, early Pubic hair and precocious puberty. • In Males: symptoms appear late except that hypokalaemia, HTN and dehydration etc. <p>Scenarios in Exam:</p> <ul style="list-style-type: none"> • Female having ambiguous genitalia + enlarged clitoris, genotype = 46 XX • OR the genotype 46XX is given with above mentioned clinical features and the diagnosis is asked that is Adrenogenital syndrome or CAH – Female Pseudohermaphrodite. 				
Testicular feminization syndrome (46 XY) or Androgen insensitivity syndrome	<ul style="list-style-type: none"> • 46, XY karyotype – Male pseudohermaphrodite → • X-linked recessive disorder • Androgen receptor resistance or receptor absent for DHT/ testosterone → \uparrow testosterone. • 5- alpha reductase def may also be there. • In peripheral tissue, testosterone will be converted by aromatase into estradiol → feminization. 				

	<ul style="list-style-type: none"> • Patients have normal testes & produce normal amounts of Mullerian-Inhibiting factor (MIF), therefore, affected individuals do not have Fallopian tubes, uterus, or proximal (upper) vagina. • External genitals remain same <p>Scenario in Exam:</p> <ul style="list-style-type: none"> • Child having Absent Uterus, Blind vagina what is genotype = 46XY – male pseudohermaphrodite • if diagnosis is asked → Testicular feminization or Androgen insensitivity syndrome
Gonadal dysgenesis	<ul style="list-style-type: none"> • XO gonadal dysgenesis (45, X0)-Turner syndrome • XX gonadal dysgenesis (46, XX) • XY gonadal dysgenesis (46 XY) - Swyer syndrome • XO/XY mosaicism (45, X/ 46, XY) → Mixed gonadal dysgenesis • Swyer's complete gonadal dysgenesis presents with elevated gonadotropins, normal uterus and vagina development but nonfunctional streak gonads, eunuchoid body habitus along with no sign of sexual development. • While in complete androgen insensitivity syndrome, uterus is absent, and vagina is blind/short

Trinucleotide Repeat Expansion Diseases

- Diseases in which the mutation is characterized by a long repeating sequence of 3 nucleotide
- Fragile X syndrome: CGG Repeats, x linked dominant, macro-orchidism with long jaw and everted ears
- Huntington's disease: CAG repeats
- Myotonic Dystrophy: CTG repeats (early balding in males, Difficulty in releasing hand shake, Cataracts)
- Friedreich's Ataxia: GAA Repeats

Mental Retardation (MR)

- The most common cause of chromosomal abnormality causing mental retardation is Down Syndrome
- The most common mendelian disorder causing mental retardation is fragile X syndrome (2nd common cause of MR)
- The irreversible cause of mental retardation is thyroid deficiency.
- The least common cause of mental retardation is Klinefelter syndrome.

Fetal Alcohol syndrome (FAS)

- results from alcohol exposure during the mother's pregnancy.
- FAS causes brain damage and growth problems that vary from child to child and are not reversible
- Facial characteristic
- Thin upper lip, short nose, Small eye-opening, small midface, small head circumference with Indistinct Philtrum

Key Points - Teratogens

- Vit A is teratogenic that may cause Neural tube defects (NTDs) and Cleft Palate
- Lithium exposure linked to Ebstein anomaly
- Warfarin exposure causes Nasal hypoplasia and fetal bleeding or agenesis of corpus callosum
- Acetylcholinesterase – most specific for NTDs
- Anomaly scan is done at 14 – 18 weeks
- Alcohol is a teratogen that may cause **Premature birth** > microcephaly along with above mentioned defects

LAB TECHNIQUE	DESCRIPTION & USES
PCR	Steps: <ol style="list-style-type: none"> 1. Denaturation: DNA heated at 95°C to separate strands 2. Annealing: Cooling the sample at 55 °C. DNA primer + Taq polymerase are added 3. Elongation: Inc the Temp to 72 °C. DNA polymerase attaches dTNPs to the strand to replicate the sequence after each primer
Blotting techniques	Mnemonics → SNoW = DRoP <ol style="list-style-type: none"> 1. Southern Blot for DNA visualization 2. Northern Blot for studying mRNA levels and splicing errors reflective of gene expression 3. Western Blot for Protein separation and identification 4. South-western Blot: identifies DNA binding proteins using label dsDNA probes
Flow cytometry	To assess size, granularity and immunophenotyping of cells commonly used for Leukemias, immunodeficiencies, maternal fetal Rh incompatibility.
Microarray	Compare the relative gene expression in 2 samples. Used for Clinical genetic testing, forensic analysis, cancer mutations, Single nucleotide Polymorphism & Copy No. Variants
ELISA	Used to detect specific antigen or antibody in pt's serum or blood sample Screening test for HIV = ELISA
Fluorescence in situ hybridization	Used for Localization of genes and visualization of chromosomal anomalies at molecular level i.e., Microdeletions, Translocation and duplications
Karyotyping	Colchicine is added to cultured cells to halt chromosomes in METAPHASE Chromosomes are stained, Numbered and ordered according to Morphology, size, arm to Length ratio and banding pattern Karyotyping is done for numerical or structural anomalies Used to detect chromosomal imbalances: Autosomal trisomy's + Sex chromosome disorders

Robertsonian Translocation

- Chromosomal translocation that commonly Involves chromosome pairs 21, 22, 13, 14 and 15.
- One of the most common types of Translocations.
- Occurs when the long arms of 2 acrocentric chromosomes (chromosomes with centromeres near their ends) fuse at the Centromere and the 2 short arms are lost.

Balanced Vs Unbalanced Translocations

- Balanced → No gain or loss of Significant genetic material and normally do Not cause abnormal phenotype.
- Unbalanced (missing or extra genes) Can result in miscarriage, stillbirth, and Chromosomal imbalances.

CHROMOSOME	ASSOCIATED CONDITIONS
Chromosome 3	Von Hippel-Lindau disease, renal cell carcinoma
Chromosome 4	ADPKD (PKD2), achondroplasia, Huntington disease
Chromosome 5	Cri-du-chat syndrome, familial adenomatous polyposis
Chromosome 6	Hemochromatosis (HFE)
Chromosome 7	Williams syndrome, cystic fibrosis
Chromosome 9	Friedreich ataxia, tuberous sclerosis (TSC)
Chromosome 11	Wilms tumour, B-globin gene defects (e.g., sickle cell disease, β-thalassemia), MEN 1 syndrome
Chromosome 13	Patau syndrome, Wilson disease, retinoblastoma (RB), BRCA2
Chromosome 15	Prader-Willi syndrome, Angelman syndrome, Marfan syndrome
Chromosome 16	ADPKD (PKD1), alpha-globin gene defects (e.g., α-thalassemia), tuberous sclerosis (TSC2)
Chromosome 17	Neurofibromatosis type 1, BRCA1, TP53 (Li-Fraumeni syndrome)
Chromosome 18	Edwards syndrome
Chromosome 21	Down syndrome
Chromosome 22	Neurofibromatosis type 2; DiGeorge Syndrome 22q11
X Chromosome	Fragile X syndrome, X-linked agammaglobulinemia, Klinefelter syndrome (XXY)

SUMMARY & IMPORTANT PAST PAPERS BCQS – ONE LINERS

1. Inc or dec No. of chromosomes instead of 46 = Aneuploidy
2. Early onset of Alzheimer's disease at 35 is associated with = DOWN Syndrome
3. 34 weeks pregnant lady having low AFP, low estriol and high HCG = DOWN syndrome
4. Difference of autosomal dominant from autosomal recessive = Heterozygous affected
5. Klinefelter's karyotype = 47XXY while Turner syndrome karyotype = 45 XO
6. Regarding Turner syndrome = Complete or Permanent X Monosomy present
7. Mode of inheritance for defective genes involved in DNA repair = Autosomal Recessive
8. Most common congenital syndrome = Down's syndrome
9. Most common sex chromosomal abnormality = Klinefelter's syndrome
10. X chromosome in male is = Hemizygous
11. Marfan syndrome is due to defective = Fibrillin (inherited defect)
12. Chromosome 15 gene defect is linked to = Marfan syndrome
13. Scanty Barr body is seen in = Turner's syndrome
14. Repeaters sequence of trinucleotides is seen in = Fragile X syndrome (CGG)
15. Cystic hygroma seen in = Turner syndrome
16. Myelomeningocele seen in = Edward syndrome
17. Polycystic kidneys seen in = Patau syndrome (P for Patau and Polycystic)
18. Horseshoe kidneys seen in = Turner syndrome
19. Genetic analysis is done with = Amniotic fluid analysis
20. Down syndrome is trisomy 21
21. Patau syndrome is trisomy 13, Edward syndrome is trisomy 18
22. XX pseudohermaphrodite = Congenital adrenal hyperplasia or Adrenogenital syndrome
23. Allele = Non identical gene at same locus
24. Most common pattern of genetic diseases = Multifactorial
25. Microcephaly + epicanthal folds + Protruded tongue = Down's syndrome
26. Boy with normal trunk and short limbs non-consanguineous marriage between parents, disease is Achondroplasia type of inheritance = Autosomal Dominant
27. Duchenne muscular dystrophy defective gene makes the cell impermeable to Protein
28. Technique used to detect localization of genes, chromosomal abnormality and microdeletion = FISH
29. Technique used to detect gene expression = Microarray
30. Prominent Occiput + Microcephaly + Small jaw = Edward's syndrome
31. One Barr body is present in = Normal female > Klinefelter syndrome
32. Short stature, webbed neck +neck lymphedema = Turner syndrome
33. Can't differentiate b/w green and red = Deuteranopia
34. Can't differentiate b/w red and green = Protanopia
35. Can't differentiate b/w Blue and green = Tritanopia
36. Retinoblastoma = AD pattern
37. Haemophilia = XR pattern. Thalassemia = Autosomal recessive. G6PD = X linked recessive
38. Long jaw + long face + Large testes = Fragile X syndrome
39. Autosomal dominant disorder with tumour mutation = Familial adenomatous polyposis
40. Chorea, mental retardation, depression and memory deficit = Huntington's chorea → Autosomal Dominant
41. When both alleles are fully expressed in heterozygote are called = Codominance
42. Most common autosomal dominant disease = Von Willebrand's disease
43. Most common autosomal recessive inheritance = Hemochromatosis
44. DM, HTN & IHD exhibit = Multifactorial inheritance
45. In AD pattern e.g., Huntington chorea = 50% children affected
46. In autosomal dominant, genetic defect if phenotypically not expressed = Reduced penetrance
47. 11 yr old child died of renal disease that showed cysts, pattern of inheritance = AR pattern
48. Gynaecomastia is a feature of = Klinefelter's syndrome
49. Part of triple screening for Down's syndrome = ESTRIL (Not estradiol)
50. Estradiol is more in pre - menopausal whereas Estrone more in Post menopausal

51. Regarding karyotype of true hermaphrodite = $XX > XX/XY > XXY$
52. Snow storm appearance is seen in = Complete Mole (46XX or 46XY)
53. For Partial mole = 69XX or 69XY may be seen
54. Colon cancer + endometrial cancer in inherited form = Hereditary non-Polyposis Colorectal cancer = Mutation of MSH – 2 or MLH – 1 (mismatch repair genes)
55. In down syndrome Robertsonian translocation transmit in how much percentage to next generation = 33%
56. Both male and female are involved in = Autosomal dominant pattern
57. A person exhibiting an extra chromosome in genes = Trisomy
58. Child with down syndrome one of parents may have = Robertsonian translocation
59. For diagnosis of thalassemia = CVS can be done
60. Best diagnostic for turner = Karyotyping
61. Best option in identification of turner syndrome prenatally = USG
62. To diagnose Neural tube defects early in pregnancy which Investigation is preferred = USG
63. Barr body may help in diagnosis of = Turner syndrome
64. Lady with Primary amenorrhea, breast present, Uterus absent and blind Vagina = 46 XY Testicular feminization syndrome or Androgen insensitivity syndrome
65. A young boy with enlarged genitals, rapid growth, excessive body hair = adrenogenital syndrome or CAH
66. If a complete chromosome is transferred to a haploid cell in Meiosis this abnormality is called = Trisomy, but the mechanism involved is Meiotic Non – Disjunction
67. A child, genetically born male but female like external genitalia = Testicular feminization syndrome
68. Mitochondrial mutation is only transferred from = Mother
69. 12 yr. old girl with primary amenorrhea, normal secondary sex characters but short blind vagina and absent uterus. The defect lies in = Paramesonephric duct (responsible for development of female reproductive organs)
70. Barr body in XXX = 2
71. Regarding AD inheritance = Incomplete penetrance present
72. Duchenne muscular dystrophy = X linked recessive
73. In a 40 yr. old female chances of Down's syndrome = 1: 100
74. In 30 yr. old risk of Down's syndrome is 1:1000, risk at 45 yr. is 1:25 – 30
75. Hereditary spherocytosis mode of transfer = AD pattern
76. Cystic fibrosis = Autosomal recessive but Alport syndrome = X linked dominant
77. Horseshoe kidney is NOT linked with = DOWN's syndrome
78. recurrent abortions or still birth with unremarkable clinical/genetic history. Investigations to be done = Karyotyping.
79. In Alcoholic mother baby is at risk of = Prematurity > Microcephaly
80. Most specific test for NTDs = Acetyl cholinesterase
81. For numerical and structural anomalies, the test to do = Karyotyping
82. Excess Vit A may cause = Neural tube defects or cleft palate
83. Regarding recombinant theory what suits = Plasmid
84. Female 45XO will have = Gonadal dysgenesis and germinal hypoplasia
85. Regarding X linked disorders = Heterozygotes are rarely affected
86. In AR pattern = disease presents in $\frac{1}{4}$ children
87. Risk of down syndrome in next baby if mother having Robertsonian translocation = 5%
88. Microcephaly with high pitched cry and cardiac anomalies = Cri – du – chat syndrome (chromosome 5p-)
89. Down syndrome clinical presentation is due to = Over expression of genes
90. In X linked recessive, sons of female carrier 50% affected and daughters 50% carriers
91. Complete penetrance and early uniform expression seen in = AR pattern
92. Vertical inheritance pattern = AD mode of inheritance
93. Horizontal pattern and male/female equally affected in = AR pattern
94. Blood groups are an example of = Codominance
95. Ataxia, prolonged laughter and seizures with low IQ = Angelman syndrome - occurs when maternal allele is mutated
96. Most common Mendelian pattern of inheritance = Autosomal recessive, overall common is Multifactorial pattern
97. Father transmits disease to all daughters but not sons in = XD pattern
98. No male – male transmission + Skips generations = X linked Recessive diseases
99. Sickle cell anaemia = AR pattern
100. Hemizygous X chromosome seen in = Turner syndrome
101. Most common X linked disorder = Fragile X syndrome

102. Most common cause of mental retardation overall = Down syndrome
103. MC congenital cause of low IQ or mental retardation = Down syndrome
104. Most common inherited cause of mental retardation = fragile X syndrome
105. Overall 2 nd common cause of mental retardation = Fragile X syndrome
106. The gene that regulates normal morphogenesis during development is = Homeobox gene.
107. All the following are characteristic of Turner Syndrome EXCEPT = Umbilical Hernia
108. Nuchal translucency is helpful in diagnosis of = Down's syndrome
109. Hypertriglyceridemia is seen in = Dysbetalipoproteinemia
110. Marfan syndrome defect in = Fibrillin – 1
111. In Marfan's syndrome, Aortic aneurysm occurs most commonly in = Ascending aorta
112. The approximate number of genes contained in the human genome is = 1,00,000
113. True about genomic imprinting = Different expression of gene depending on parent of origin
114. Advanced paternal age → Neurofibromatosis, Marfan syndrome, Klinefelter syndrome
115. Advanced maternal age → Down syndrome, XXX syndrome, Klinefelter syndrome
116. Mitochondrial inherited Diseases: Leber, Hereditary Optic neuropathy, MELAS Syndrome
117. MELAS = Mitochondrial encephalopathy, lactic acidosis, stroke like syndrome
118. Presence of Red ragged fibres are helpful in establishing the diagnosis of MELAS.

IMMUNOLOGY

Primary Immune system organs	<ol style="list-style-type: none"> 1. Bone marrow: immune cell production, B cell maturation 2. Thymus: T cell maturation
Secondary immune organs	<ul style="list-style-type: none"> ○ Spleen, lymph nodes, tonsils, Peyer patches ○ Allow immune cells to interact with antigen

Lymph node	<ul style="list-style-type: none"> ○ Lymphoid organ that has many afferents, 1 or more efferent. Encapsulated, with trabeculae. ○ Functions are nonspecific filtration by macrophages, circulation of B and T cells, and Immune response activation. it has follicles, medulla, and, paracortex. <table border="1"> <tr> <td>Follicles</td><td> <ul style="list-style-type: none"> ○ Site of B-cell localization and proliferation in outer cortex. 1° follicles are dense and quiescent. 2° Follicles have Pale central germinal centres and are active. </td></tr> <tr> <td>Medulla</td><td> <ul style="list-style-type: none"> ○ Consists of medullary cords (closely packed lymphocytes and plasma cells) and medullary sinuses. ○ Medullary sinuses communicate with efferent lymphatics, contain reticular cells & Macrophages </td></tr> <tr> <td>Para-cortex</td><td> <ul style="list-style-type: none"> ○ Contains T cells. Region of cortex between follicles and medulla. ○ Contains high endothelial Venules through which T and B cells enter from blood. ○ Paracortex is Not well developed in patients with DiGeorge syndrome. ○ Paracortex enlarges in an extreme cellular immune response (e.g., EBV and other viral infections – Paracortical hyperplasia → lymphadenopathy </td></tr> </table>	Follicles	<ul style="list-style-type: none"> ○ Site of B-cell localization and proliferation in outer cortex. 1° follicles are dense and quiescent. 2° Follicles have Pale central germinal centres and are active. 	Medulla	<ul style="list-style-type: none"> ○ Consists of medullary cords (closely packed lymphocytes and plasma cells) and medullary sinuses. ○ Medullary sinuses communicate with efferent lymphatics, contain reticular cells & Macrophages 	Para-cortex	<ul style="list-style-type: none"> ○ Contains T cells. Region of cortex between follicles and medulla. ○ Contains high endothelial Venules through which T and B cells enter from blood. ○ Paracortex is Not well developed in patients with DiGeorge syndrome. ○ Paracortex enlarges in an extreme cellular immune response (e.g., EBV and other viral infections – Paracortical hyperplasia → lymphadenopathy
Follicles	<ul style="list-style-type: none"> ○ Site of B-cell localization and proliferation in outer cortex. 1° follicles are dense and quiescent. 2° Follicles have Pale central germinal centres and are active. 						
Medulla	<ul style="list-style-type: none"> ○ Consists of medullary cords (closely packed lymphocytes and plasma cells) and medullary sinuses. ○ Medullary sinuses communicate with efferent lymphatics, contain reticular cells & Macrophages 						
Para-cortex	<ul style="list-style-type: none"> ○ Contains T cells. Region of cortex between follicles and medulla. ○ Contains high endothelial Venules through which T and B cells enter from blood. ○ Paracortex is Not well developed in patients with DiGeorge syndrome. ○ Paracortex enlarges in an extreme cellular immune response (e.g., EBV and other viral infections – Paracortical hyperplasia → lymphadenopathy 						
Spleen	<ul style="list-style-type: none"> • Periaarteriolar sheath: Contains T cells. Located within white pulp. • Follicles: Contains B cells. Located within white pulp. • Marginal Zone: Contains macrophages and specialized B cells, here, the antigen-presenting cells capture blood-borne Ag for recognition by lymphocytes. Located between red pulp and white pulp. • Red pulp: role in Spleen immunological filtration. • White pulp: role in Spleen immunological function. • Worn out RBCs come at → red Pulp and sinusoids. • Marginal Zone: Ag presenting portion. • Post- Splenectomy findings: Thrombocytosis > Howel Jolley bodies, Target cells, Lymphocytosis. • In asplenia: Risk of infection with encapsulated organisms Like Pneumococcus, H. Influenzas, N. Meningitis. 						
Thymus	<ul style="list-style-type: none"> • It is not directly involved in response to foreign antigens. • Paracellular connection is present in thymus. • It is in the anterosuperior mediastinum and Site of T-cell differentiation and maturation. • Thymus epithelium is derived from third pharyngeal pouch (endoderm). • Thymic lymphocytes are of mesodermal origin. Cortex is dense with immature T cell. • medulla is pale with mature T cells and Hassall corpuscles containing epithelial reticular cells. • Normal neonatal thymus "sail-shaped" on CXR. • T cell maturation in Thymus and B cell maturation in Bone marrow. • Thymoma is the neoplasm of thymus. Associated with myasthenia gravis, superior vena cava. syndrome, pure red cell aplasia, Good syndrome. • Remember: Reticular cells present in Thymus > dermis. 						
Key Facts	<ul style="list-style-type: none"> • Subcapsular sinuses are present in Lymph Node. • Paracortex of lymph node is poorly developed in DiGeorge syndrome. • Spleen immunological filtration occurs at: Red Pulp and worn-out RBCs come at Red Pulp & Sinusoids. • Howel – Jolly body is a post splenectomy finding. • Paracellular communication occurs in Thymus. • B cells form and mature inside bone marrow. • T cells form in bone marrow and mature in thymus (T for T cell & Thymus). • Cortex of thymus is dense with immature T cells. • Periaarteriolar sheath present in spleen contains T cells. 						

Innate immunity	<ul style="list-style-type: none"> Germ line encoded, Non-specific immunity that occurs rapidly in minutes – hours, having No memory. It consists of: Physical barriers (Skin, mucous membranes), Neutrophils, Macrophages & Monocytes, NK cells That collectively secrete enzymes (Lysozymes), cytokines, complement proteins, CRP, defensins. Toll like receptors and pathogen recognition receptors associated with Pathogen associated molecular patterns help in recognition of pathogens. Pathogenic associated Molecular patterns are Lipopolysaccharide (gram – ve bacteria), Flagellin of bacteria and Nucleic acids of viruses 				
Adaptive Or Acquired immunity	<ul style="list-style-type: none"> Highly specific immunity that develops during life over longer periods, initially slower response than innate immunity but memory response of adaptive type is faster. Adaptive immunity varies through recombination during lymphocyte development. Adaptive immunity consists of T cells, B cells. T cells secrete cytokines while B cells form Circulating antibodies or immunoglobulins Memory cells formed from B & T cells. B cells form Plasma cells that secrete antibodies Memory cells: B + T cells form Memory cells in response to previously encountered antigens and these cells create faster & quicker response. Types of Acquired immunity are: <ol style="list-style-type: none"> Active Acquired – may be natural or artificial. Passive Acquired – may be natural or artificial. <table border="1"> <tr> <td>Active immunity</td><td> <ul style="list-style-type: none"> Immunity developed after being exposed to an infection or getting vaccinated. Types are: Natural active immunity: antibodies made after exposure to infection e.g., URTIs. Artificial-active immunity: antibodies made after getting a vaccination e.g., DPT, Polio vaccine </td></tr> <tr> <td>Passive immunity</td><td> <ul style="list-style-type: none"> Immunity acquired from mother or by administration of anti-sera. Types are: Natural passive immunity: antibodies transmitted from mother via placenta or milk. Artificial passive immunity: antibodies acquired from immune serum e.g., anti-tetanus serum </td></tr> </table>	Active immunity	<ul style="list-style-type: none"> Immunity developed after being exposed to an infection or getting vaccinated. Types are: Natural active immunity: antibodies made after exposure to infection e.g., URTIs. Artificial-active immunity: antibodies made after getting a vaccination e.g., DPT, Polio vaccine 	Passive immunity	<ul style="list-style-type: none"> Immunity acquired from mother or by administration of anti-sera. Types are: Natural passive immunity: antibodies transmitted from mother via placenta or milk. Artificial passive immunity: antibodies acquired from immune serum e.g., anti-tetanus serum
Active immunity	<ul style="list-style-type: none"> Immunity developed after being exposed to an infection or getting vaccinated. Types are: Natural active immunity: antibodies made after exposure to infection e.g., URTIs. Artificial-active immunity: antibodies made after getting a vaccination e.g., DPT, Polio vaccine 				
Passive immunity	<ul style="list-style-type: none"> Immunity acquired from mother or by administration of anti-sera. Types are: Natural passive immunity: antibodies transmitted from mother via placenta or milk. Artificial passive immunity: antibodies acquired from immune serum e.g., anti-tetanus serum 				

Antigen presenting cells (APCs)	<p>They express MCH – II on surface and express Co - stimulatory signals for T helper cells activation. Following are Typical APCs:</p> <ol style="list-style-type: none"> Dendritic cells (Professional Ag presenting cells) and Langerhans cells Macrophages B cells
Antigen processing	It is the process by which pathogens and their Products are degraded to produce peptide Antigens
Antigen presentation	These peptide fragments combine with MHC Molecules inside cells. The MHC-peptide complex thus formed travels to the cell surface where it displays peptide fragments to T cells. This is known as Antigen Presentation.
MAJOR HISTOCOMPATIBILITY COMPLEX (MHC)	
MCH is encoded by HLA genes (Human Leukocyte antigen) which present antigens to T cells by binding T cell receptor	
Similarities b/w MHC I, II	<ul style="list-style-type: none"> Both are synthesized in rough endoplasmic Reticulum, found on the surface of APC surface, and are encoded by genes in HLA locus. In both class I and class II, expression of genes is Co-dominant
Key differences b/w MHC I, II	<ul style="list-style-type: none"> MHC – I binds with CD8+T cells while MHC – II Binds with CD4+ Cells. MHC – I presents Endogenous antigen (Viral proteins) MHC – II presents Exogenous Antigen (Ag) e.g., bacterial products. Remember the rule of 8; MHC – I × CD 8 = 8; MCH – II × CD 4 = 8

MHC-I	MHC-II
<ul style="list-style-type: none"> Encoded by HLA – A, HLA – B, HLA – C Have 8-10 amino acids and Peptide binding domain: Alpha1, alpha2, has no invariant chain. Composed of one peptide, Encoded in HLA locus and beta 2 Microglobulin. Found on all surfaces of Nucleated cells, APCs, Platelets and Placental Trophoblastic tissue. MHC – I Presents antigen to CD 8+ T- cells and binds with endogenous antigen – Viral or cytosolic products. After binding to CD8 T- cells, cytokines are Produced that lead to the Lysis of entire cell. 	<ul style="list-style-type: none"> Encoded by HLA locus – D, (DP, DQ, DR) Found on surface of APCs and Activated T cells. Have 13-18 amino acids and Peptide binding domain: alpha1 & Beta1 (2 equal length chains) Composed of two peptide and has invariant chain. Presents antigen to CD 4 T-cells and binds with exogenous antigen (bacterial proteins) After binding to CD4 T cells, it triggers B cell response Which results in antibody formation

HLA	Association with diseases
HLA-B27	PAIR = Psoriatic arthritis, Ankylosing spondylitis, IBD-associated arthritis, Reactive arthritis Order of association of HLA – B27: Ankylosing Spondylitis > Reactive arthritis > Psoriatic arthritis
B5	Behcet's disease
B57	Abacavir hypersensitivity
DQ2/DQ8	Celiac disease
DR2	Multiple sclerosis, hay fever, SLE, Goodpasture syndrome
HLA-DR3	DM type.1, SLE, Graves' disease, Hashimoto's Thyroiditis, Addison disease
HLA-DR4	Rheumatoid arthritis, DM type 1, Addison Disease
HLA-DR5	Hashimoto's thyroiditis, Pernicious anaemia

Natural killer cells (NK Cells)	<ul style="list-style-type: none"> Member of innate immune system. Use perforin and granzymes to induce apoptosis of viral infected and Tumour cells. Activity is enhanced by IL-2, IL-12, IFN-a, and IFN-B. Has CD 16, for Ab dependant cell mediated cytotoxicity
B-lymphocytes (20%)	<ul style="list-style-type: none"> Mediate Humoral immune response by production of antibodies. Contribute to Immunological immune response by producing memory cells.
T-lymphocytes (80%)	<ul style="list-style-type: none"> They mainly Mediate Cell-mediated immunity. Humoral Immunity by TH1 cells & IFN – Gamma Cellular Immunity by TH2 cells & IL – 4 CD4 T cells help B cells make antibodies and produce cytokines to recruit phagocytes and activate other leukocytes. CD8+ T cells directly kill virus infected + tumour cells by perforin and granzymes like NK Cells Mediate the Delayed cell-mediated hypersensitivity (type IV). Participate in Acute and chronic cellular organ rejection

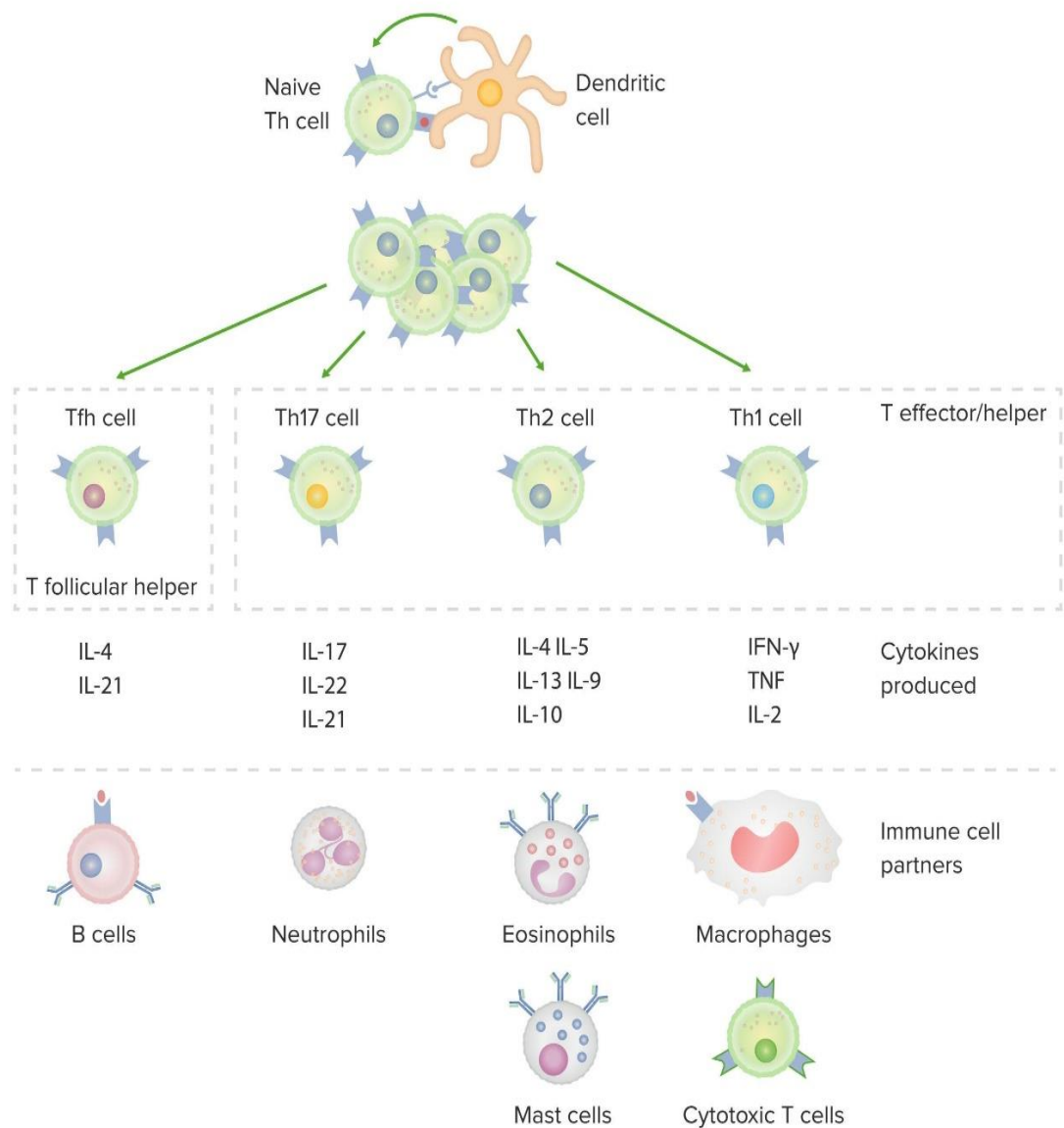
DIFFERENTIATION OF T CELLS

<ul style="list-style-type: none"> Positive Selection occurs in Thymic cortex. T cells expressing T cell receptors (TCRs) capable of binding self-antigens on MHC on cortical epithelial cell Survive Negative Selection occurs in Thymic Medulla. T cells expressing TCRs with high affinity for self-antigens undergo apoptosis or Become regulatory T cells, Tissue-restricted self-antigens are expressed in the thymus due to the Action of autoimmune regulator (AIRE). AIRE Deficiency leads to autoimmune polyendocrine syndrome 1; Chronic mucocutaneous candidiasis, Hypoparathyroidism, Adrenal insufficiency, Recurrent candida infections are the features. T Helper cells have CD4+, binds to MCH-II. Cytotoxic T cells Kill virus-infected, neoplastic, and donor graft cells by inducing apoptosis, release cytotoxic granules containing preformed Perforin & granzyme. Cytotoxic T cells have CD8, which binds to MHC I on virus-infected cells. Regulatory T cells Help maintain specific immune tolerance by suppressing CD4" and CD 8 T-cell effector function, Identified by expression of CD3 CD4, CD25 and FOXP3.

Activated regulatory T cells (T regs) produce anti-inflammatory cytokines (IL-10, TGF-B)

CELL SURFACE RECEPTORS

T cells	<ul style="list-style-type: none"> TCR (binds antigen-MHC complex) CD3 (associated with TCR for signal Transduction) CD28 (binds B7 on APC) Helper T Cells: CD4, CD40L, CXCR4/CCR5 (co-receptors for HIV) Cytotoxic T Cell: CD8 Regulatory T Cells: CD4, CD25
B cells	Ab (binds antigen) CD 19, CD20, CD21 (receptor for EBV), CD40, MHC II. B7
Macrophages	CD14 (receptor for PAMPs e.g., LPS), CD40 CCR5, MHC II, B7 (CD80/86) Fc and C3b receptors (enhanced phagocytosis)
NK cells	CD 16 binds Fc of IgG). CD56 (suggestive Marker for NK)
Hematopoietic stem cells	CD 34



Summary – Important Cytokines source & Role

- Macrophages secrete TNF, IL 1, IL 6, IL 8 & IL 12.
- T Cells generally secrete IL – 2, IL – 3.
- TH1 Cells secrete IFN – Gamma, IL 17, 21, 22 -contribute to acute inflammation.
- TH2 Cells secrete IL – 4, 5, 6, 10, 13.
- Antigen Presenting cells secrete IL- 12 → activates TH1 → produce IFN-Gamma → activate Macrophages + CD8 cells.
- IFN- Gamma activates Macrophages and they secrete: TNF, IL 1, IL 6, IL 8 & IL 12.
- IFN- Gamma activates TH1 & Macrophages and inhibits TH2, TH17, Induces Granuloma formation.
- IL- 2 activates TH2 & T regulatory, generally all T cells.
- IL3 Stimulates Bone marrow.
- IL- 4 Promotes growth of B cells, activates TH2 & inhibits TH 1, TH17, enhances class – switching to IgE & IgG
- IL – 5 Promotes growth & differentiation of B cells + Eosinophils, enhances Class switching to IgA
- IL – 10 Anti-inflammatory action
- IL – 13 Activates classic macrophage activation to promote Healing process.
- IFN-a, IFN-B, IFN-Y** are part of innate host defence, interferons interfere with both RNA and DNA viruses.
Uses: Chronic HBV, Kaposi sarcoma, hairy cell leukaemia, condyloma acuminatum, renal cell carcinoma, malignant melanoma, multiple sclerosis, chronic granulomatous disease.
Side effects are Flu-like symptoms, depression, "neutropenia, 'myopathy, interferon-induced autoimmunity.
- Anergy** is the state during which a cell cannot become activated by exposure to its antigen.
- T and B cells become anergic when exposed to their antigen without costimulatory signal (signal 2) -another Mechanism of self-tolerance.

IMMUNOGLOBULINS (ANTIBODIES - Ab)

- Antibodies Are gamma globulins Synthesized by plasma cells and Constitute 25-30 % of total serum proteins.
- Antibodies are present in serum, tissue Fluids and mucosal surfaces.
- All antibodies are immunoglobulins, but all Immunoglobulins may not be antibodies.
- Functions include Opsonization, do Complement activation and Neutralization (preventing adherence of bacteria)

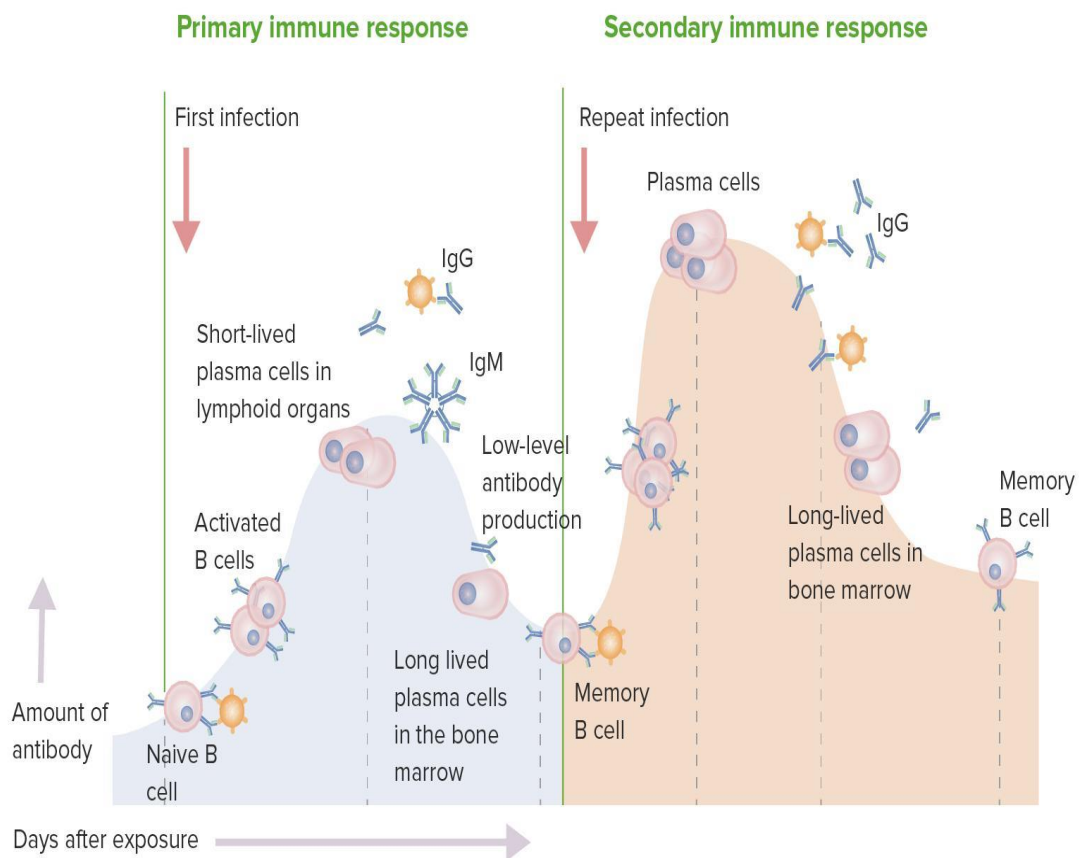
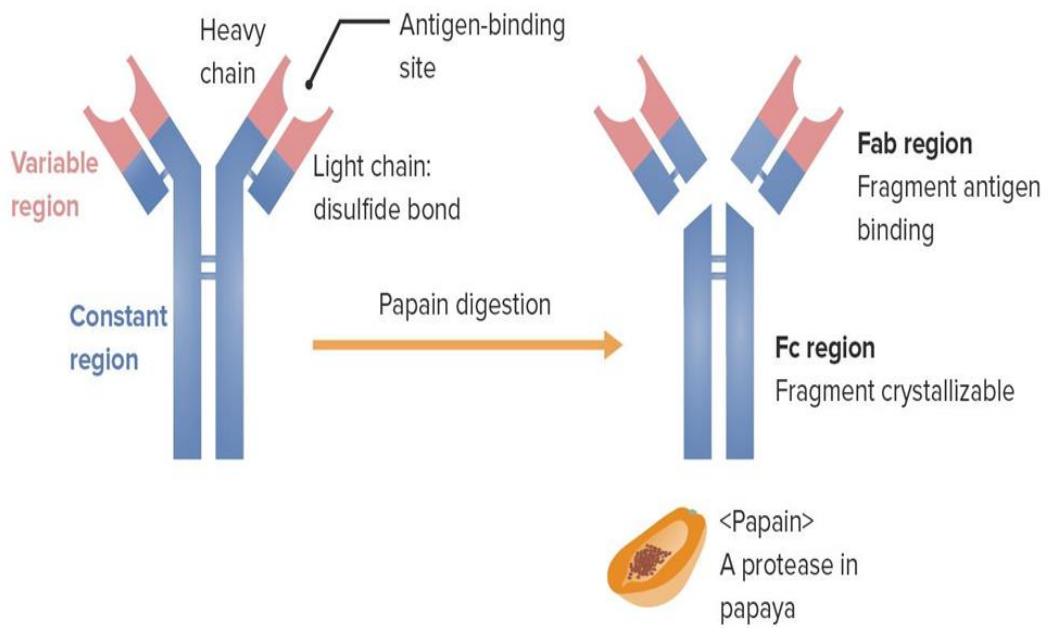
Structure (Light & Heavy chains)

- Composed of 4 polypeptide chains; 2 identical light and 2 identical Heavy chains, Linked by disulphide bonds.
- Light chains similar in all Immunoglobulins. Light chains occur in 2 Varieties kappa and lambda.
- Light and Heavy chains are Subdivided into variable and Constant region.
- Each heavy and light chain Contains amino terminal in Variable region.
- Carboxy Terminal in constant region
- Heavy chains are structurally and antigenically distinct for each class.
- Heavy Contributes only to Fab region, Light Chains contribute to both Fab & Fc portions.**
- Each immunoglobulin peptide Chain has intra chain Disulphide bonds- form loops.
- Each loop is compactly folded to form a globular structure- Domain.
- Light chain contains a single Variable domain (VL) and a Single constant domain (CL).
- Heavy chain contains one Variable domain (VH) and 3 Constant domains (CH1, CH2 CH3)**
- Hinge region is the segment in Heavy chain - between CH1, CH2

Functional regions (Fab & Fc regions)

Fab region	<ul style="list-style-type: none"> Fragment, antigen binding, consisting of light (L) and heavy (H) chains, recognizes antigens. Fab is a unique antigen-binding Pocket that Determines idiootype: only 1 antigenic specificity expressed Per B cells
Fc region (5 C's)	<ul style="list-style-type: none"> Constant Carboxy terminal Complement binding (Fc Portion of IgM & IgG fixes complement) Carbohydrate side chains Confers (determines isotype (IgM. IgD) Functionality or biological activity of antibody mainly dependant on Fc portion Heavy chain contributes to Fc region

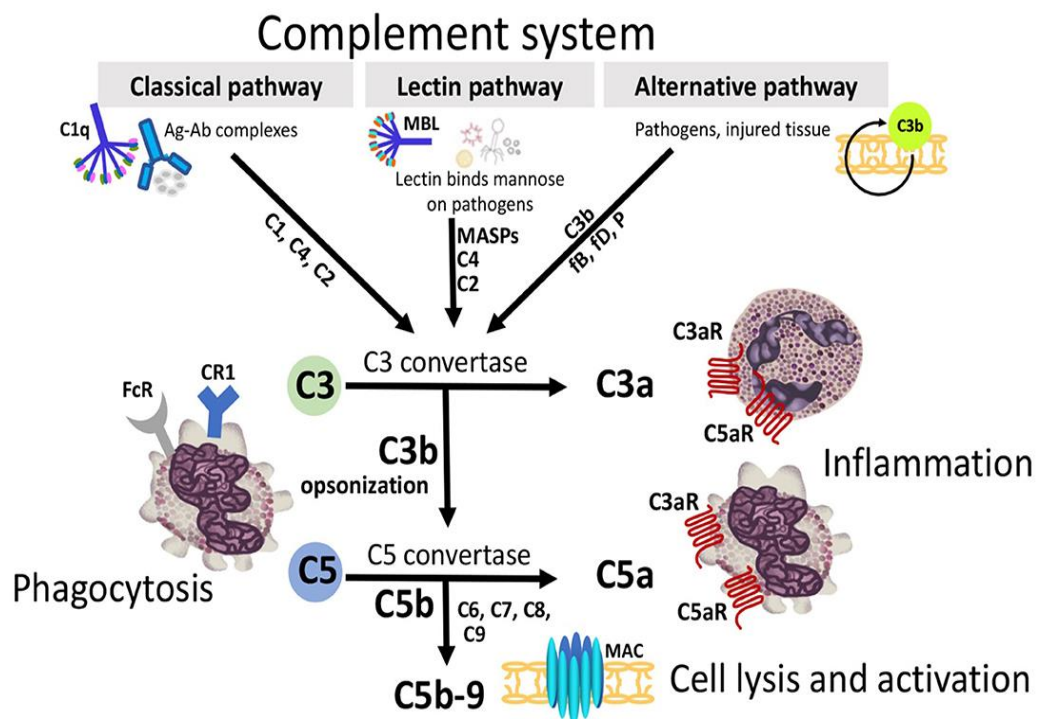
Generation of Ab diversity	<p>Key word = Random recomb or addition, antigen-independent</p> <ul style="list-style-type: none"> • Random recombination, of VJ (light-chain) Or V(D)J (heavy-chain) genes • Random addition of nucleotides to DNA during recombination by terminal Deoxynucleotidyl transferase (TdT) • Random combination of heavy chains with Light chains
Generation of Ab specificity	<ul style="list-style-type: none"> • Antigen dependant • Somatic hypermutation and affinity Maturation of variable region • Isotype switching (constant region)
Classification of antibodies (GAME-D)	
<ul style="list-style-type: none"> • All isotopes can exist as monomers. • Mature, naive B cells express IgM & IgD on their surface prior to activation. • These B cells differentiate into plasma cells in germinal centre of lymph nodes to secrete IgA, IgE & IgG. • IgG: Protects the body fluids. • IgA: Protects the body surfaces • IgM: Protects the blood stream • IgE: Mediates type I hypersensitivity • IgD: Role not known 	
IgG	<ul style="list-style-type: none"> • 75 – 80 % Concentration in serum- most abundant in serum • It is the Ab of Chronic infection. Persists throughout life to give lifelong immunity • Cross placenta and provide natural immunity to foetus and neonate at birth • Act against bacteria and virus by opsonizing • Activates complement by classic pathway • 4 IgG subclass, the serum concentration of IgG-1 subclass is highest (60-70%) • Protect the body fluids
IgA	<ul style="list-style-type: none"> • 15% in body but Most Abundant Ig produced in body (in the submucosa) • IgA inhibits binding of adhesive substances to the mucosal surface- Protects the body surface • Present in colostrum, breast milk, saliva, tear, mucus of respiratory tract digestive tract and genitourinary tract. In serum exist as a monomer, in external secretion exist as a dimer • Activate complement by the alternate pathway
IgM	<ul style="list-style-type: none"> • 5% in body, Protects the bloodstream. It is the Ab of Acute infection • The Earliest immunoglobulin to be synthesized by foetus. • The only way to identify a Neonatal infection serologically is by detection of pathogens specific IgM antibodies. This is Because the foetus receives IgG antibodies from the mother by active transport across the Placenta • IgM is by far largest antibody in the human circulatory system • IgM is present on B cells and its main function apparently is the control of B-cell activation • Its pentameric structure gives 10 free antigen binding sites and possesses a high Avidity.
IgE	<ul style="list-style-type: none"> • < 1 % in body • Mediate type 1 hypersensitivity reaction. IgE protect against the Parasitic worm. • Highest carbohydrate and least concentration in body. IgE is bound to mast cell and basophils cell
IgD	<ul style="list-style-type: none"> • 2%, Present in serum on B cells, Function is Unclear.
Key Facts	<ul style="list-style-type: none"> • Order of Concentration in serum or body: IgG > IgA > IgM > IgD > IgE. (GAM – DE) • Complement Fixation: IgM > IgG3 > IgG1 > IgG2 > IgG4. • Placenta Crossing: IgG 1 > IgG 3 > IgG 4 • To check acute infection in neonate: IgM • Antibodies need to be tested in case of infection or to detect infection: IgG. • Note the difference b/w acute inf and just infection.



COMPLEMENT SYSTEM

- System of hepatically synthesized plasma proteins that play Role in innate immunity, aids immune system in defence against microbes and has role in Inflammation.
- Membrane attack complex (MAC) defends against gram -ve bacteria.
- The CH50 test Is used to screen for activation of the classical complement pathway.

Three complement pathways	<ol style="list-style-type: none"> 1. Classic (IgG or IgM mediated) → (Antigen – antibody complexes) involves C1, C2, C4 2. Alternative: microbe surface molecules → Involves C3b mainly 3. Lectin binding mannose or other sugars on microbe Surface → C1 like
Functions	<ul style="list-style-type: none"> • opsonization (also Fc region of IgG) → Opsonin's enhance phagocytosis. • C3b binds to lipopolysaccharides on bacteria. • C3a, C4a, C5a—anaphylaxis • C5a—neutrophil chemotaxis • C5b-9 (MAC): cytotoxicity. • MAC complex- important for neutralizing Neisseria spp, Deficiency results in Recurrent infection. • Inhibitors -decay-accelerating factor (DAF Aka CD55) and C1 esterase inhibitor help Prevent complement activation on self-cells (e.g., RBCs).
Disorders	<ul style="list-style-type: none"> • Early complement Deficiencies (C1-C4): Recurrent pyogenic and Respiratory tract infections • C3 clears Ag-Ab complexes, so its deficiency may result in SLE. • Terminal complement Deficiencies (C5-C9)- Inc Risk of recurrent Neisseria infections • Complement regulatory protein deficiencies: • C1 esterase inhibitor deficiency causes hereditary angioedema due to unregulated activation of kallikrein – bradykinin, Characterized by low C4 levels. ACE inhibitors are contraindicated in it • Paroxysmal nocturnal Hemoglobinuria is due to defective PIGA gene that prevents formation of GPI anchors for complement inhibitors such as decay accelerating factor (DAF/CD55) and CD59 <p>Presents with; Complement mediated intravascular haemolysis, low haptoglobin, dark urine</p>



HYPERSENSITIVITY REACTIONS (HSR)	
Four types of HSR exist: Mnemonics = ACID → Atopy, Cytotoxic, immune mediated, Delayed type	
Type I HSR	<ul style="list-style-type: none"> • TYPE I = Atopy, Allergy, Asthma (AAA) • Antibody: IgE. Response time: 15-30 min • Free antigen cross-links IgE on pre-sensitized mast cells and basophils, triggering the release of Vasoactive amines that act at post-capillary venules (i.e., histamine). • Reaction develops Rapidly after antigen exposure because of preformed antibody. • Tryptase is marker of Mast cell activation. <p>Examples:</p> <ul style="list-style-type: none"> • Anaphylaxis like some bee sting, some food/drug allergies, iodinated contrast media, Beta-lactam antibiotics (e.g., penicillin) and Hymenoptera stings • Allergic and atopic disorder (e.g., Rhinitis, Hay fever eczema, Hives, Asthma) • Blood transfusion reaction is type 2, but in IgA deficient individuals it is type 1 reaction.
Type II HSR	<ul style="list-style-type: none"> • Response time is Minutes to hours. • Cytotoxic (Antibody-mediated): IgM, IgG bind fixed antigen on enemy cell leading to cell destruction. • Mechanism: Antibodies bind to cell-surface antigens → Cellular destruction, inflammation, and Cellular dysfunction. <p>A. Cellular destruction: cell is opsonized (coated) by antibodies leading to either:</p> <ol style="list-style-type: none"> a. Phagocytosis and/or activation of Complement system. b. NK cell killing (antibody-dependent cellular Cytotoxicity). <p>Examples: Autoimmune Haemolytic anaemia, ITP, Haemolytic disease of newborn, Blood transfusion reactions</p> <p>B. Inflammation: binding of antibodies to cell Surfaces, activation of complement system and Fc receptor-mediated inflammation Examples: Good Pasteur syndrome, Rheumatic fever & Hyperacute graft rejection</p> <p>C. Cellular dysfunction: antibodies bind to cell Surface receptors lead to abnormal blockade or Activation of downstream process. Examples: Myasthenia gravis, Pemphigus vulgaris.</p>
Type III HSR	<ul style="list-style-type: none"> • Antibody: IgG, IgM. Response time: 3-8 Hours • Immune complex antigen-antibody complex activate complement, which attracts neutrophil. • Neutrophil release lysosomal enzymes • Examples: Serum sickness & Arthus reaction, Post streptococcal glomerulonephritis, PAN, SLE, Shick test, Henoch – Schlein purpura. • Serum Sickness: the prototypic immune Complex disease. Antibodies to foreign proteins Are produced and 1-2 weeks later, antibody-Antigen complexes form and deposit in tissues. Complement activation – inflammation and tissue damage (low serum C3, C4) • Arthus reaction: a local subacute immune Complex-mediated hypersensitivity reaction Intradermal injection of antigen into a pre-sensitized (has circulating IgG) individual Leads to immune complex formation in the Skin (e.g., enhanced local reaction to a booster Vaccination). Characterized by edema fibrinoid necrosis, activation of complement
Type IV HSR	<ul style="list-style-type: none"> • Main cells are T-cells and macrophages. Response time: 48-72 hours. • Delayed cell-mediated hypersensitivity reaction. • The Response is delayed and does not involve antibody. • Examples: Tuberculin reaction. Crohn's disease, Rheumatoid arthritis, Lepromin test, Chronic graft rejection, Multiple sclerosis, Temporal arteritis & Contact dermatitis, Poison Ivy, nickel allergy.

BLOOD GROUPS

ABO Blood group	Blood Group	Antigen (On RBC)	Antibody (In Plasma)
	A	A	B
	B	B	A
	O	H	A, B
	AB	A, B	NONE

	<p>Key Concepts</p> <ul style="list-style-type: none"> • ABO gene is on chromosome 09 while HLA gene on chromosome 06. • ABO blood group is an example of Codominance. • ABO blood types in human are determined by three alleles. • For Blood grp antigens: Remember this sequence. Present on RBCs surface > Glycoproteins > Equally immunogenic. • Blood group is of same type as the type of antigen e.g., A blood grp has Antigen A, but Antibody present will be Opposite i.e., B anti body in blood grp A. • +ve blood grp can donate blood to +ve only but -ve blood grp can donate to both -ve and +ve groups. • Blood grp AB+ is Universal recipient – as it lacks A, B antibodies. • Blood group with no agglutinin: AB + ve. • Blood grp O -Ve is Universal donor of blood. • If there is insufficient time to do cross Matching of blood, give O+ve to Males and O -ve to females. • O +ve is present in 47% Caucasians. • Plasma exchange or Exchange transfusion is done with – ve blood of the same type. E.g., for exchange transfusion of AB+ grp → AB -ve grp is recommended. • Most severe reaction: A +ve to O +ve (past paper BCQ). • Adverse blood transfusion occurs in: AB – ve to A + ve. • Mother blood group A, one child O and other child AB, father will have blood group: B group. • Rh factor Present on RBC, many Rh antigens are present but only the Rh D is the most immunogenic.
Bombay blood group	<ul style="list-style-type: none"> • The antigen present on O group red cell is the H substance, which is precursor of A and B antigens. • Absence of H substance leads to a rare blood group termed that is the Bombay blood Group designated as “Oh”. These individuals have anti-A, anti-b and anti-H antibodies and can receive blood only from individuals with Bombay blood group
MNS group	<ul style="list-style-type: none"> • MNS blood groups are determined by their reaction with Anti-M, Anti-N and Anti-S • These blood group rarely causes haemolysis following transfusion

BLOOD TRANSFUSION	
	<ul style="list-style-type: none"> • Cross-matching of blood is required to prevent transfusion reaction. • Cross-matching of blood Takes about 45 minutes in most laboratories. • Packed cells are stored in a SAG-M solution to increase the shelf life to 5 weeks at 2-6 °C. • Multiple or Repeated long term blood transfusion can cause Hemochromatosis, mostly Seen in Thalassemia pt. • If a patient needs multiple blood transfusion for surgery, the ideally crossmatch should be done After every bag. • In an anesthetized patient sign of transfusion reaction are oozing and hypotension.
Hb levels & transfusion	<ul style="list-style-type: none"> • Hb less than 6gm/dl, transfusion will benefit the patient. • 6-8 g/dl = transfusion unlikely to be benefits in the absence of bleeding or surgery. • > 8gm/dl= no indication for blood transfusion.
Complications of transfusion	<ul style="list-style-type: none"> • Hypothermia may lead to cardiac arrhythmia including fibrillation and asystole. • For this reason, Blood warming is necessary if the blood transfusion rate exceeds 50ml/min. • But Blood is warmed primarily to cause right shift of Oxygen dissociation curve.

- Hyperkalaemia may occur in stored blood, potassium level increase by 1meq/L/day, not a problem Unless a very huge amount of blood is given quickly.
- **Massive transfusion** is defined as the replacement of total blood volume within a 24-hour period or about 5L in adult.
This can lead to Hypocalcaemia; excess citrate can act on the Patient plasma free ionized calcium and result in hypocalcaemia.
- Massive transfusion may cause: **Hyperkalaemia**, hypokalaemia, Hypocalcaemia and Hypothermia.
- **Multiple transfusion** may cause **Hypocalcaemia**, Hyperkalaemia and Hypokalaemia.
- **Repeated transfusion** may cause Iron overload (in patient with Thalassemia) or **hemochromatosis**.

BLOOD TRANSFUSION REACTIONS

Most common cause for a major haemolytic transfusion reaction is clerical error (Human error)

Such as mislabelled specimen sent to the blood bank, or not properly identifying the patient to whom You are giving the blood. Following types of blood transfusion reaction may occur, as explained below

Allergic or anaphylactic reaction	<ul style="list-style-type: none"> • Occurs Within minutes to 2 – 3 hrs after transfusion due to release of preformed inflammatory mediators from mast cells. • It is a Type 1 hypersensitivity reaction against plasma protein of transfused blood. • Severe reaction in IgA deficient individuals, must receive blood products lacking IgA. • Clinical features: urticaria, pruritis, itching common at infusion site, wheezing, fever. Treatment: stop, observe and antihistamine. • In case of anaphylaxis Clinical features are Dyspnoea, bronchospasm, hypotension, respiratory arrest, and hypotension. Treatment: stop the transfusion, Epinephrine and IV fluids.
Febrile non-haemolytic reaction	<ul style="list-style-type: none"> • Occurs in 1 – 6 hrs, due to preformed cytokines released by donor WBCs. • Host antibodies against donor HLA antigen and leukocytes. • Clinical features: Fever, Headache, Chills and flushing. • May be prevented by leukoreduction of blood products.
Acute haemolytic transfusion reaction (ATHR)	<ul style="list-style-type: none"> • During or within 24 hrs of transfusion due to preformed antibodies (ABO incompatibility) • Clinical features: <ul style="list-style-type: none"> • Fever, important early sign, Hypotension, rapidly leading to shock, Tachypnoea, Tachycardia, Flank pain and bleeding at transfusion site • Hemoglobinuria – intravascular haemolysis typically and Jaundice – extravascular haemolysis • In anaesthetic patient: <ul style="list-style-type: none"> • Tachycardia, hypotension and oozing from the surgical site • Acute haemolytic transfusion reaction due to transfusion of incompatible blood in A patient under general anaesthesia usually presents as generalized bleeding due to DIC. • The most specific tests to determine haemolysis are free plasma haemoglobin And Hemoglobinuria • Treatment: <ul style="list-style-type: none"> • Stop transfusion. • Hydration to maintain urine output >100ml/hour. • Diuresis with Mannitol to prevent renal failure.
Transfusion related acute lung injury (TRALI)	<ul style="list-style-type: none"> • Occurs Within minutes to 6 hrs due to anti HLA Ab in donor blood. • These anti HLA Ab or anti leukocytic Ab activate neutrophils that are sequestered in pulmonary vasculature. • neutrophils release mediators that cause increase Capillary Permeability → Pulmonary edema. • Present with dyspnoea, respiratory burst and non-cardiogenic pulmonary edema.

Delayed haemolytic reaction	<ul style="list-style-type: none"> Anamnestic response to A foreign antigen on Donor RBCs (Rh [D] or Other minor blood group Antigens) previously Encountered by recipient. Typically causes extravascular haemolysis over 24 hrs (usually 1 - 2 weeks) that is self-limited and presents with mild fever and hyperbilirubinemia or it may be clinically silent.
------------------------------------	--

BLOOD LOSS

- In Vaginal delivery, normal blood loss: 500 ml, C-section blood loss is 1000 mL approx.
- Normal blood loss during the first week Post partum is another 800 ml.
- Return to non-pregnant circulating volume in-3-4 week post-delivery.
- Shock occurs when > 20% or = 1000 ml blood volume loss occurs and there is no change when Blood loss is about 500 ml
- 10-15 % blood loss should be replaced by Ringer lactate (R/L)
- Normal menstrual flow is < 80 ml.
- After haemorrhage plasma is restored in 24 hrs (12 – 72 hrs).
- Plasma proteins return to normal in 2-3 days and RBC return in the last-4-8 weeks.
- RBCs are last to return after haemorrhage.
- Least lymphatic flow is due to haemorrhage.
- The Best measure of blood loss estimation is the weight of soaked gauze.
- Hb of 6g/dl is acceptable in patient who are not actively bleeding, not about to Undergo major surgery and are not symptomatic.

TRANSPLANTATION

Graft	<ul style="list-style-type: none"> Graft are tissues that are transferred without their blood supply. Therefore, they must be re-vascularized once they are at a new site.
Flap	<ul style="list-style-type: none"> Flaps are tissues that are transferred with a blood supply. They have the advantage of bringing vascularity to the new area. Free flaps: The blood supply has been isolated, disconnected, and then Reconnected using microsurgery at the new site.
Autograft	<ul style="list-style-type: none"> Graft taken from self. It has the best survival rate.
Isograft	<ul style="list-style-type: none"> From identical twin or clone and it is always accepted.
Allograft	<ul style="list-style-type: none"> From non-identical individuals of same species.
Xenograft	<ul style="list-style-type: none"> Graft taken from different species.
Orthotopic graft	<ul style="list-style-type: none"> A graft placed in its normal anatomical site e.g., Orthotopic liver transplant.
Heterotopic graft	<ul style="list-style-type: none"> A graft placed in a site different from that where the organ is Normally located.
Key Facts	<ul style="list-style-type: none"> Cornea transplant is the most successful transplant. ABO blood grouping is the first important or earliest/initial prerequisite for successful transplantation. HLA is the main trigger of graft rejection and thus HLA is the Most important for transplant. For Bone marrow transplant HLA is more important as they lack ABO system. Best Site for HLA matching/typing: Buccal mucosa. Best tissue for HLA matching/typing: Bone marrow. Best cell or blood cell for HLA Typing: WBC. For kidney transplant, HLA-1 is more important, for liver transplant - ABO is important. HLA typing in renal transplant decreases the activation of CD8. The most common reason for skin graft failure is hematoma beneath the graft. There is no need of immunosuppressant drugs for graft taken from an identical twin. Antigen-antibody reactions are most reduced in liver failure (due to hypogammaglobulinemia). In emergency, For Liver and Heart transplantation HLA matching is not required. RBCs are washed to prevent hypersensitivity or allergic reaction.

TRANSPLANT REACTIONS

Hyperacute rejection (Type II HSR)	<ul style="list-style-type: none"> ➤ Type II HSR, may occur Within minute and is irreversible. ➤ It is due to the presence in the recipient of pre-formed antibodies against HLA- class 1 antigen. ➤ It can also occur due to ABO-blood group incompatibility. ➤ Kidney transplants are particularly vulnerable to Hyperacute rejection. ➤ Heart and liver transplant are relatively resistant. ➤ Widespread Thrombosis of graft vasculature occurs with ischemic and fibrinoid necrosis. ➤ Graft must be removed.
Acute rejection (Type II/IV HSR)	<ul style="list-style-type: none"> ➤ It usually occurs during the first 6 months (typically between first week and 3 months ➤ May be acute cellular type (CD8/CD4 mediated) or acute humoral type (antibodies mediated). ➤ It may be of type II HSR or type 4 HSR. ➤ Acute cellular is reversible with immunosuppressants. ➤ Vasculitis of graft vasculature occurs in acute rejection.
Chronic rejection (Type II+IV HSR)	<ul style="list-style-type: none"> ➤ Occurs in Months to year, type II + type IV HSR and it is the most common type of reaction. ➤ The liver appears to be more resistant. ➤ Chronic rejection is the most common cause of allograft failure, and It is Irreversible ➤ T-cell and antibodies mediated vascular damage occurs dominated by Arteriosclerosis. ➤ Recipient T cells react and secrete cytokines causing atrophy and fibrosis of graft. ➤ Examples: Chronic Allograft nephropathy and Accelerated atherosclerosis of Heart
Graft vs Host disease (Type IV HSR)	<ul style="list-style-type: none"> ➤ Type IV HSR in which Donor T cells reject host cells. Usually occur in bone marrow or liver transplant ➤ Present with Maculopapular rash, Jaundice, Hepato-splenomegaly and Diarrhoea (specific feature) ➤ On labs, Hyperbilirubinemia > hyperamylasaemia can be the findings. ➤ Irradiation of blood products before transplant reduces risk of GVHD

COMPLICATIONS OF TRANSPLANT

Infection	<ul style="list-style-type: none"> • Transplant recipients are a high risk of opportunistic infection, especially by viruses. • Viral infection may result from reactivation of latent virus or from primary infection. • CMV is the most common infection in transplant patients (e.g., Heart) • CMV doesn't not predispose transplant patient to malignancy. • Candida albicans is the most common infection in solid organ transplantation- causes Angular cheilosis. • BK virus (Polyoma virus) infection is most common in Renal transplants. • The risk of bacterial infection is highest during the first month after transplantation. • Pneumocystis carinii is the most common Protozoal infection seen after transplantation.
Malignancy	<ul style="list-style-type: none"> ➤ risk is particularly high for those type of tumour in which viral infection plays an etiological role. ➤ The risk is particularly high for skin cancer and a condition called post-transplant. Lymphoproliferative disorder (PTLD). Most of the skin cancers PTLD are associated with EBV. ➤ Most common malignancy post-transplant is the skin cancer. ➤ 5 Years or less, more risk of Lymphoproliferative disorder. ➤ Skin - Squamous cell carcinoma may occur frequently especially after 10 years.
Renal transplant	<p><u>The Incidence in renal transplant:</u></p> <ul style="list-style-type: none"> • Lymphocele: 50% - The most common. • Renal artery stenosis 10% while Renal artery thrombosis < 1%. • Renal vein thrombosis <1%.

IMMUNODEFICIENCY

A state in which Immune system's ability is compromised or entirely absent to fight against infectious diseases and cancer

Types of Immunodeficiency disorders:

	Primary or inherited disorders	Due to defect in immune system component According to component system defect may be in: <ol style="list-style-type: none">B cells defects – 50% (most common) they include X linked agammaglobulinemia, Common variable immunodeficiency, Selective IgA deficiency.T Cells disorders:DiGeorge syndrome, hyper IgE or Job's syndrome, Chronic mucocutaneous candidiasisCombined B & T cell disorders: Severe combined immunodeficiency disease, Ataxia telangiectasia, hyper IgM syndrome and Wiskott - Aldrich syndromeComplements system deficiencies: C1Q, Factor H, D, I or Properdin deficiency.Phagocytic defects: Chronic granulomatous disease, Leukocyte adhesion defects, Chadiak Higashi syndrome and Myeloperoxidase deficiency
	Secondary or acquired	Non-immunogenic or non-immune causes e.g., malnutrition, malignancy, prematurity, injury, burns, splenectomy, drugs (steroids) and transplant pts.
Etiological classification	<ul style="list-style-type: none">▪ Congenital (X-linked disease).▪ Acquired (AIDS): discussed in detail in Microbiology section.▪ Idiopathic.▪ Embryogenesis (DiGeorge syndrome).	
Age of presentation	<ul style="list-style-type: none">• Onset before age 6 months of age suggests a T-cell defect.• Onset between the age of 6-12 months suggests Combined B- and T-cell defects or a B-cell defect.• Later than 12 months usually suggests a B-cell defect or Secondary immunodeficiency.	
Major Pattern of Microorganisms causing infections in immunodeficiency		
	<ul style="list-style-type: none">• B Cells deficiencies produce bacterial infections more• T cell disorders may cause Viral and fungal infections frequently	
Low B cells	<ul style="list-style-type: none">▪ Encapsulated bacterial infections; Strep Pneumoniae, H. Influenza, Neisseria meningitidis.▪ Enteroviral encephalitis, Polio virus infection and giardiasis etc	
Low T cells	<ul style="list-style-type: none">▪ Bacterial sepsis, chronic Viral respiratory and GI infections, CMV, EBV etc.▪ Local candidiasis, Pneumocystis and cryptococcal fungal infections	
Low B & T cells	<ul style="list-style-type: none">▪ Chronic multiple viral, bacterial, fungal & protozoal infections▪ Low Granulocytes → Bacterial infections mainly, Systemic candidiasis & aspergillus.▪ No Viral infections	
Complement deficiencies	<ul style="list-style-type: none">▪ Early complement deficiencies (C1-C4) → Encapsulated bacterial infections e.g., pneumococcus.▪ Late Complement deficiencies:(C5-C9) → Neisseria spp infection	

PRIMARY IMMUNE DEFICIENCY DISORDERS		
B cell disorders	X linked or Bruton's Agammaglobulinemia	<ul style="list-style-type: none"> X-linked recessive – more in boys, Defect in BTK, a tyrosine kinase gene B cell maturation defect that Presents after 06 months of age with: Recurrent bacterial and enteroviral infections Absent Lymph nodes and tonsils. Absent germinal centre in Lymph nodes. Absent B cells in peripheral blood Decreased or absent Immunoglobulins (Ig) of all classes Live Vaccines -- contraindicated
	Common variable immunodeficiency	<ul style="list-style-type: none"> Unknown cause in most cases- B cell differentiation defect Present in adults' life (15 - 35 yr.) with: Sinopulmonary infections, Bronchiectasis, Diarrhoea Inc risk of autoimmune diseases and lymphoma Decreased plasma cells and low Immunoglobulins levels
	Selective IgA deficiency	<ul style="list-style-type: none"> Most common primary immunodeficiency – unknown cause Mostly asymptomatic May present with Respiratory and GI infections (Giardiasis) Inc risk of autoimmune diseases Hypersensitivity to blood products i.e., type 1 HSR in IgA deficiency. Dec IgA, normal IgG and IgM
T cell disorders	Thymic aplasia	<p>22q11 microdeletion, failure to develop 3rd and 4th Pharyngeal pouches. Absent Thymus and parathyroids</p> <p>CATCH-22: Cardiac defects (conotruncal abnormalities [e.g., tetralogy of Fallot, truncus Arteriosus), Abnormal facies, Thymic hypoplasia</p> <p>T-cell Deficiency (recurrent viral and Fungal infections), Cleft Palate</p> <p>Hypocalcaemia, Parathyroid aplasia, Tetany</p> <p>DiGeorge syndrome: Thymic, parathyroid and cardiac defects, thymic shadow absents on CXR, ↓ PTH, Ca+2 and T cells.</p> <p>Velocardio-facial syndrome: Palatal, facial and cardiac defects</p>
	Hyper IgE or Job's syndrome	<ul style="list-style-type: none"> Deficiency of Th17 cells due to STAT3 mutation. Impaired recruitment of neutrophils to sites of infection. Features include Cold (noninflamed) Staphylococcal Abscesses, Retained Baby teeth, Coarse Facies, eczema and Bone Fractures trauma, minor trauma. IgE levels and eosinophils raised.
	Chronic mucocutaneous syndrome	<ul style="list-style-type: none"> T cell dysfunction. <p>Impaired cell-mediated immunity against Candida spp.</p> <p>Classic form caused by defects in AIRE that presents with:</p> <p>Endocrinopathy along with Skin and nail infections.</p>
Combined B & T cell disorders	Severe combined immunodeficiency (SCID)	<p>Several types including:</p> <ol style="list-style-type: none"> Defective 1L-2R gamma Chain (most common X-linked recessive) Adenosine Deaminase deficiency (Autosomal recessive) RAG mutation – VDJ Recombination defect <p>Clinical Features and Diagnosis:</p> <ul style="list-style-type: none"> Failure to thrive, Chronic Diarrhoea and Thrush Recurrent viral, bacterial. Fungal and protozoal Infections T-cell receptor excision Circles (TRECs) Part of newborn screening for SCID Absence of thymic shadow (on CXR)

		<ul style="list-style-type: none"> Absent germinal centres (lymph node biopsy) and T cells (flow cytometry)
	Wiskott-Aldrich syndrome	<ul style="list-style-type: none"> Mutation in WAS gene; X-linked Recessive Leukocytes and platelets Unable to reorganize actin Cytoskeleton defective Antigen presentation WATER = Wiskott-Aldrich, Thrombocytopenia, Eczema, Recurrent (pyogenic) Infections risk of autoimmune disease and malignancy Dec to normal IgG, IgM, Low IgE, IgA, Fewer and smaller platelets
	Hyper IgM syndrome	<ul style="list-style-type: none"> X-linked recessive Class switching defect. Most commonly due to Defective CD40 L on T helper cells Severe Pyogenic infections Early in life Opportunistic Infection with pneumocystis, Cryptosporidium and CMV Normal or increase IgM and low IgG, IgA and IgE due to Failure to make germinal Centers
Phagocytic defects	<p>Chronic granulomatous disease: absent neutrophil NADPH oxidase, recurrent infections with catalase +ve organisms e.g., Staph aureus, klebsiella, candida, aspergillus.</p> <p>Abnormal tetrazolium test.</p> <p>Others: Chediak Higashi syndrome and LAD deficiency – discussed in inflammation & Repair section</p>	

When to suspect of Immunodeficiency Disorders?

- Infections with unusual organisms (e.g., Aspergillus)
- Infections of unusual severity (e.g., varicella Complicated by pneumonia)
- Infections occurring at unusual sites (e.g., liver Abscess)
- Clinical manifestations of a specific immune Disorder (e.g., DiGeorge anomaly)
- Family history of immunodeficiency
- Recurrent infections

VACCINES

Type of Vaccine	Description & Examples
Live attenuated	<ul style="list-style-type: none"> Microorganism rendered non-pathogenic but retains capacity for transient growth within inoculated host that Induce cellular and humoral responses Provides strong often Lifelong immunity. Also, may revert to virulent form hence, contraindicated In Pregnant and Immunodeficient patients. <p>Examples:</p> <ul style="list-style-type: none"> Adenovirus (attenuated Given to military recruits) Typhoid (Ty21a, oral), Polio (Sabin), varicella (chickenpox), smallpox BCG, Yellow fever, Influenza (Intranasal), MMR, Rotavirus <p>Note: MMR and varicella vaccines can be given to people living with HIV without evidence of immunity if CD4 cell count >200 cells/mm³</p>
Killed	<ul style="list-style-type: none"> Pathogen is inactivated by heat or chemicals. Maintaining Epitope structure on surface antigens is important for immune response. Mainly induces a humoral response. They are safer than live vaccines but generate weaker immune Response so booster shots are required. <p>Examples: Hepatitis A, Typhoid (Vi polysaccharide intramuscular), Rabies, Influenza, Polio (Salk)</p>
Toxoids	<ul style="list-style-type: none"> Denatured bacterial toxin with an intact receptor binding site. Stimulates the immune system to make antibodies without potential for causing disease. Provide Protection against the bacterial toxins.

	<ul style="list-style-type: none"> • But antitoxin levels decrease with the time that may require a booster. • Examples: Clostridium tetani and Corynebacterium diphtheriae
Subunits	<ul style="list-style-type: none"> • Includes only the antigens that best stimulate the immune system. • lower chance of adverse reactions but expensive and generate weaker immune response. • Examples: • HBV (antigen = HBsAg), HPV (types 6, 11, 16,18), Acellular pertussis (aP). • Neisseria meningitidis (various strains), Streptococcus Pneumoniae & Haemophilus influenza.
Preferred Route for Vaccines	
All vaccine are given intra-muscular Except; MMR= subcutaneously, BCG= intra-dermally and Polio = oral	
Dose of Vaccines	
<p>All vaccines are given 0.5 ml Except BCG= 0.05 ml, Polio= two drops</p> <p>In children who have not vaccinated during infancy and are still below the age of 5 years, vaccine is as follow: BCG = once, while DT and Polio Drops: 2 doses at 6 weeks interval and first booster 6months later</p>	

Key Facts - Vaccines

- Influenza vaccine and yellow fever vaccine contain egg protein -- contraindicated in egg Allergy people
- If convulsion occurs within 72 hours of DPT injection further administration of pertussis vaccine is contraindicated Then, give DT alone.
- After 2 years of age, children should not receive the pertussis vaccine.
- In the event of epidemics or high risk, the measles vaccine can be given at 6 months of age.
- Immunization should be delayed only in case of illness with high-grade fever, so that any sign of the illness will not be attributed to the vaccination.
- Live vaccine should not be administered to children with immune-deficiency disease.
- Meningococcal, pneumococcal and H. Influenzae type-b vaccine are polysaccharide vaccines.
- Maternal antibodies, which are transported through the placenta, protect the infants up to Age of 3-4 months.
- Antibodies against measles persist up to 6-9 months of age, if the mother has been vaccinated or suffered from measles. Therefore, measles vaccination in children should be started after that Age.
- Contraindication to the measles vaccine includes anaphylactic reaction to neomycin, anaphylactic Reaction to gelatine, pregnancy, known immunodeficiency and long-term immune-suppressive Therapy.
- Transfer of maternal antibodies via the placenta is an example of passive immunization.
- Intravenous Immune Globulin (IVIG) is a human blood product consisting of antibodies, which are Used to treat immunodeficiency disorders, B-cell chronic lymphocytic leukaemia, inflammatory demyelinating disorders.
- There are two types of polio vaccine, oral (Sabin) an injectable (Salk) vaccine, both contain three strains.
- OPV which is used in EPI is bivalent. Even if the child has suffered from poliomyelitis. He should be vaccinated to protect him Against other two types of polioviruses and for herd immunity.
- **Rotavirus vaccine** is used to protect against rotavirus infections - The leading cause of severe diarrhoea among young children.

It is now included in the EPI schedule as a 10th vaccine.

Administered in two oral doses for children of 6 weeks as well as 10 weeks of age, it will help Reduce the diarrhoea related mortality in children below five. The interval between the two doses at least 4 weeks.

The first dose of Rotavirus Vaccine cannot be given if the child is older than 16 weeks of age.

Small risk of Intussusception from Rotavirus vaccination usually within a week after 1st or 2nd dose.

- Immunity Given by Vaccine e.g., DPT/BCG is Artificial Active
- Contraindicated in child with Seizure is - DPT.
- Inactivated toxin Used as Toxoid in Tetanus. Active immunity given Tetanus toxoid is 100% effective.
- MMR Vaccine is Live Attenuated
- Tetanus Vaccine is Inactivated Toxin
- Pertussis Vaccine – Whole cell (Killed organisms) 78-80 % effective and Acellular Vaccine is 71-85% Effective.
- Rubella vaccine given in reproductive age.
- MMR contraindicated in Pregnancy, Anaphylaxis and Immunodeficiency
- Hypersensitivity to Vaccines e.g., DPT is Type III HSR. Hypersensitivity to Tb vaccine is Type IV HSR

Autoantibody involved	Associated disorder
Anti-postsynaptic Ach receptor	Myasthenia gravis
Anti-presynaptic voltage gated Ca channels	Lambert-Eaton myasthenic syndrome
Anti B2 glycoproteins 1	Anti phospholipid syndrome
ANA	Initial test for SLE (screening)
Anti Smith, Anti-ds DNA	SLE (anti-smith more specific)
Anti cardiolipin, Lupus anticoagulant	Anti phospholipid syndrome in SLE
Anti histone	Drug induced Lupus
Anti U1 RNP (ribonucleoprotein)	Mixed connective tissue disorder
Anti CCP	Most Specific for Rheumatoid arthritis
Rheumatoid factor (IgM against Fc of IgG)	Rheumatoid arthritis (initial test)
Anti Ro (SSA); Anti La (SSB)	Sjogren syndrome
Anti Scl-70 (anti DNA topoisomerase I)	Diffuse scleroderma
Anti centromere antibody	Limited Scleroderma (CREST syndrome)
Ant synthetase (anti SRP, anti-Helicase - anti-Mi-2)	Polymyositis, dermatomyositis
Anti mitochondrial antibody (AMA)	Primary biliary cirrhosis (PBC)
Anti-smooth muscle, anti-liver/kidney Microsomal	Autoimmune Hepatitis
C-ANCA (PR3- ANCA)	Wagner granulomatosis
P-ANCA (MPO-ANCA)	Microscopic polyangiitis, Churg Strauss syndrome, Ulcerative colitis, 1° sclerosing cholangitis
Primary membranous nephropathy	Anti-phospholipase A2 receptor
Anti-hemidesmosome antibody	Bullous pemphigoid
Aini-desmoglein (anti-desmosome)	Pemphigus vulgaris
anti thyroglobulin, anti-thyroid peroxidase (anti microsomal)	Hashimoto thyroiditis
Anti-TSH receptor or TSIs	Graves' disease
IgA anti-endomysial, IgA anti-tissue Transglutaminase, IgA and IgG deamidated Gliadin peptide	Celiac disease
Anti-parietal cell, anti-intrinsic factor (more specific)	Pernicious anaemia
Anti-glutamic acid decarboxylase, islet cell Cytoplasmic antibodies	Type 1 diabetes mellitus
Anti glomerular basement membrane	Goodpasture syndrome

LABORATORY INVESTIGATIONS IN IMMUNOLOGY

- **Direct combs test** detects antibodies bounded to RBCs.
- **Indirect combs test** detects production of anti-RBC Ab.
- **Direct fluorescent antibody test (DFA)**: DFA identifies Ag in tissues.
- ELISA is a screening test for HIV while **Western blot** is a confirmatory test for HIV.
- **Multiple washing technique is used in ELISA.**
- **Flow cytometry** analyses cell populations in a complex mixture.
- **CD: The cluster of differentiation** (also known as cluster of designation or classification Determinant and often abbreviated as CD) is protocol used for identification & Investigation of cell surface molecules providing targets for immunophenotyping of cells.

SUMMARY + PAST PAPER BCQS – ONE LINERS

1. After 05 months of renal transplant, patient present with renal failure and symptoms are reversed by immunosuppressive therapy = Acute Cellular graft rejection (Acute cellular rejection resolves with treatment)
2. NK cell's function is =To Kill cancerous and virus infection cells (note the word infected not effected)
3. Repeated episodes of viral and bacterial infections in a pt, what is the finding = T cell disorder (decreased cells in paracortex of thymus → DiGeorge syndrome)
4. A Child presented in cardiac OPD with cardiac defect, cleft palate and psychiatric behaviour = DiGeorge syndrome
5. Newborn with hypocalcaemia, tetany, cleft palate and bacterial or fungal infections = DiGeorge syndrome (22q deletion)
6. 8months old baby with Respiratory (sinusitis, Pneumoniae) and GIT infections and decreased Ig of all classes =
7. X linked/Bruton agammaglobulinemia → No Tonsils + absent germinal centre in lymph nodes
8. A boy with respiratory + GIT infections and dec immunoglobulins and plasma cells = Common Variable Immunodeficiency CVID (age group → 15 – 35 with sinopulmonary infections)
9. Thymus contain capsule but no lymphatic nodule.
10. AIDS effects TH1 cells CD4+
11. Classical pathway via IgM plus IgG while Alternate pathway by IgA plus IgG.
12. Most common primary immunodeficiency = Selective IgA deficiency
13. IV immunoglobulins provide = Passive Immunity (artificial passive)
14. Fever in infection (e.g., appendicitis) is mediated via Cytokines (IL1 & TNF)
15. Cytokines mediate fever through Prostaglandins.
16. Small displacement of antibody in radioimmunoassay of hormone due to = Increased/Excessive antibody response
17. HLA typing is done to prevent = Rejection
18. Xenograft = graft from different species
19. Transplant or graft rejection between HLA identical siblings = Minor Histocompatibility complex (not major)
20. First test to be done in transplant = ABO compatibility, while most important test for transplant = HLA Matching or typing
21. For liver transplant = ABO compatibility is imp but For Renal transplant most imp test = HLA Typing
22. Post streptococcal glomerulonephritis has = Type III HSR but Contact dermatitis = Type IV HSR
23. Anaphylaxis after penicillin injection or bee sting = Type I HSR
24. IL 3 Stimulates RBCs growth.
25. Acute rejection is via = CD8+ (Type IV HSR) and Chronic rejection is via = CD4 cells (type 2+4 HSR)
26. Graft versus host disease – GVHD = Type IV HSR
27. After transplant pt presented with Rash, diarrhoea, jaundice and raised LFTs = GVHD – Diarrhoea is prominent feature
28. HLA B – 27 Associated with = Ankylosing spondylitis > Reiter syndrome (Uveitis, Urethritis and arthritis)
29. HLA B51 is linked to Bechet's disease.
30. HIV becomes latent in = Lymph nodes and spleen
31. HSR reaction in SLE = Type III HSR
32. Regarding complement fixation: IgM > IgG3 > IgG1 > IgG2 > IgG4
33. Agglutinins are = Glycoproteins
34. In Parasitic infections the Ig to be raised = IgE (e.g., in Liver fluke infestation)
35. Patient presented with recurrent cervical lymphadenopathy and infections, each time Klebsiella pneumoniae was isolated. Most likely disease = Chronic granulomatous disease (NADPH Oxidase deficiency)
36. Skin rash + Urticaria = Type I HSR
37. Antibodies in Rh – incompatibility = Complement mediated
38. Child with infection e.g., toxoplasmosis which antibody to be tested by ELISA = IgG2 > IgG1
39. Child with acute infection = test IgM Antibodies
40. MHC function = Immune Recognition
41. Antigen binding site = Hypervariable region of both Heavy and Light chains
42. Biological activity of antibody is due to = Fc portion
43. Schwartzman reaction = Endotoxin mediated
44. Regarding anti D Ab = Causes haemolytic disease of newborn > Present in Rh – ve individuals
45. B cells produce and mature in Bone marrow. T cells produce in bone marrow but mature in thymus
46. A blood group has = Anti B antibodies of IgM variety
47. ABO blood has IgM Antibody whereas Rh group has IgG Antibody
48. Antibodies in myasthenia gravis = IgG and type II HSR

49. T lymphocytes activate MCH-II by IF gamma
50. Atypical cells in infectious mononucleosis are = Activated T cells, but Infectious mononucleosis infects B cells
51. Diphtheria infects CD8+ cells.
52. A PPD or tuberculin test done in a pt and 10mm erythema seen, cells responsible=Helper T cells (CD4+)
53. Atopic asthma CBC will show=Eosinophilia
54.
55. In mismatches blood transfusion, secondary blood transfusion reaction = Hemoglobinuria
56. Erythroblastosis fetalis has which type of HSR = Type II HSR
57. After renal transplant pt presented with cyanosis and organ failure in 10 minutes, the cause is = Antibody mediated reaction → preformed Ab in Hyperacute graft rejection
58. If the Question is asked like that, after renal transplant anuria occurs and tenderness at graft site, Suitable pathogenesis is = Thrombus at transplant site
59. Rash on arm of a pt grew for 04 days and then subsided after 02 weeks = Type IV HSR
60. Cells commonly involved in graft rejection = CD8
61. HLA DR – 4 is linked to = Rheumatoid arthritis
62. HLA DR – 3 is linked to = Type 1 DM
63. Child with recurrent infections, deficient antibody = IgA deficiency
64. Newborn with recurrent infections = IgG deficiency
65. Factor that plays no role in immunity = Plasminogen
66. Concentration of IgG = 75%, IgA = 15%, least concentration is of IgE
67. During inflammation T cells bind with MHC (Not HLA)
68. Imp antigen involved in graft rejection = HLA
69. APCs showing massive phagocytic effect = Macrophages
70. Antigens Appear on RBCs at 20 th weeks.
71. Anti-tumour cells and part of innate immunity = NK cells
72. Anti-cancer cells are = NK cells > CD 8
73. Sjogren syndrome marker = Anti SSA, Anti SSB
74. Least chance of rejection in LIVER transplant
75. Pentavalent immunoglobulin or Ig with 10 binding sites = IgM → largest molecule/size
76. Immunoglobulin test is diagnostic for = Hydatid disease
77. Most imp cells for specific or adaptive immunity = Lymphocytes (helper T cells)
78. Imp cells of chronic inflammation = Macrophages
79. Abundant cells of chronic inflammation = Lymphocytes
80. M Bands are produced by Plasma cells
81. Memory is produced in specific immunity after = 03 weeks
82. Complement components are synthesized by = Hepatocytes
83. IL – 6 is most specific indicator for chorioamnionitis.
84. Cells lines seen in type 1 HSR = Mast cells (not eosinophils)
85. IgE is present on surface of Mast cells + Basophils (prefer Mast cells)
86. mast cells present in tissues and Basophils in Blood
87. Autoimmune disease against single organ = Hashimoto's Thyroiditis
88. IgG crosses placenta (IgG1 > IgG3 > IgG 4 > IgG2)
89. Basophilia is a rare condition seen in CML.
90. In Tuberculin test → type 4 HSR & T – 1 helper cells are involved.
91. In atopic asthma foreign substance reacts with = Mast cells
92. DPT provides = artificial active immunity
93. Most common cause of negative PPD or Mantoux test = IMMUNOSUPPRESSION
94. MC opportunistic infection after renal transplant = Polyoma virus (BK Virus)
95. 1 st antibody produced and short half-life = IgM
96. MHC – 1 is also present on Trophoblasts
97. MHC – 1 present ENDOGENOUS antigen to CD8+ cytotoxic cells
98. HLA – D is most imp for transplant
99. Class switching of IgG is due to IL – 4 and IFG
100. Least important for transplant = SEX of donor

101. Best survival rate is of AUTOGRAFT.
102. ISOGRAFT don't need any immunosuppression
103. CD8 prevents CMV infection post-transplant
104. HLA genes present on chromosome 6
105. GVHD is commonly seen in allogenic bone marrow transplant > Liver
106. Child with eczema, low PLT and respiratory infections = Wiskott – Aldrich syndrome
107. Most common manifestation of autoimmune disease = haematological
108. Good pasture shows = Type II HSR
109. All vaccines show type III HSR Except Tb vaccine → type IV HSR
110. Imp test for autoimmune disease = ANA. Screening or basic initial test for SLE = ANA
111. Most specific for SLE = Anti Smith Ab > Anti ds DNA
112. Dryness of mouth + dryness of eye = Sjogren syndrome
113. Mother milk contains high concentration of = IgA
114. Mother milk is notoriously deficient in iron and Vit C (If vit is asked then choose vit C > Vit D)
115. The antigens processed by exogenous epitope presentation pathways are presented with = MHC II
116. No antibodies involved in = Type IV HSR
117. T cell responsible for which disease = DM Type – 1 (Type IV HSR)
118. C3b is an = Opsonin
119. Transfusion Related acute lung injury (TRALI) Occurs in = 6 hrs
120. Pt of renal transplant is likely to develop = Polyoma infection > CMV
121. Skin graft is successful in Agammaglobulinemia
122. Which can directly induce antibody response without helper T cells involvement = Bacterial Lipopolysaccharide (LPS) e.g., Flagellin. Because LPS is a B cell activator, Not T cells
123. Blood transfusion reaction is a type of = Type II HSR
124. Spleen immunological function = white Pulp
125. Transplant from identical twin = ISOGRAFT
126. Imp Test for transplant = HLA typing. Best blood cell for HLA typing = WBCs
127. Best tissue for HLA sampling = Bone marrow. Best site for HLA typing = Buccal mucosa
128. Immunoglobulins given to an HBV needle prick pt is example of = Passive Immunity
129. Toll like receptors are linked to = Innate immunity
130. Gamma globulins are produced by = Plasma cells while Gamma globulins are produced in = Spleen
131. Gamma globulins are NOT synthesized in = Liver
132. Pregnant lady - recurrent abortions and thrombosis, autoimmune disease associated = Antiphospholipid syndrome
133. Prozone phenomena = Antibody excess (increase serum Ab titres, a false -ve reaction)
134. Low affinity for MHC – I, differentiate in thymus to form = CD8
135. Rich source of Histamine = Mast cells
136. Fever in Pseudomonal infection is caused by = TNF
137. Microglial cells are = Antigen presenting cells in brain
138. Regarding Basophils = cells having Dense granules and IgE on their surface
139. Delayed cell mediated HSR = Tb, Contact dermatitis, Poison Ivy and nickel allergy
140. Malar rash in a pt with ANA +ve, which investigation can be done = Serum Complement levels (C3 & C1 decrease)
141. Feature of secondary immunodeficiency = Failure of immune responses
142. Professional APCs are = Dendritic cells
143. Involvement of splenic follicles with tapioca like granules = Sago spleen
144. Involvement of splenic sinusoids + Red pulp = Lardaceous spleen
145. Myasthenia gravis and pure red cell aplasia is linked to = Thymoma
146. Passive immunity has memory of = 03 weeks
147. Normal CD4:CD8 ratio = 2: 1 (ratio is > 1)
148. Thymus is not directly involved in response vs foreign antigens
149. Paracellular connections are present in = Thymus
150. CD = Cluster of Differentiation
151. CD31 cell that secretes perforin and granzyme = Cytotoxic T cell
152. CD56 cell secreting perforin and granzyme = NK cell
153. A product of Vaccination is = Memory B cells

154. A cell producing large quantities of antibody but doesn't express surface Ig = Plasma cell
155. A cell that expresses both IgM and IgD on surface = Naive mature B cell
156. Cells residing in liver part of reticuloendothelial system = Kupffer cells
157. Cell derived from monocytes that attach to arterial intima and accumulate lipids = Foam cells
158. A syncytial cell found in granuloma = Giant cell
159. Eosinophilia + raised IgE, low IgA = Job's syndrome (T Cell disorder)
160. A cytokine produced by Th1 cells and promote cell mediated immunity = IF gamma
161. A cytokine produced by Th2 cells and promote humoral immunity = IL – 4
162. A Tissue resident cell responding to PAMPs and release Histamine = Mast cell
163. Anti-inflammatory cytokine = IL – 10
164. A cytokine produced by Macrophages that induces liver production of acute phase proteins = IL – 6
165. A Pt presented with transfusion reaction after well cross matches blood indicates = IgA deficiency (type 1 HSR)
166. 11-month-old child with esophageal candidiasis, chest infection pneumocystis, thin thymus, diminished lymph nodes and no absent germinal centre = ADA deficiency (SCID)
167. Defect in neutrophils NADPH oxidase system produce = Chronic granulomatous disease
168. IF beta is used in Multiple sclerosis treatment
169. IF – alpha is used in Hep-B & C, Kaposi sarcoma and malignant melanoma.
170. Farmer lung disease is due to = Grain dust (Organic)
171. Host doesn't need to worry about rejection of transplant in = SCID
172. Abundant Ig present in body = IgG
173. Ig that is abundantly produced in body = IgA
174. Ig in sero-mucinous glands: IgG and IgA
175. Ig in primary immune response = IgM
176. Ig in secondary immune response = IgG
177. Ig with maximum sedimentation rate = Ig M → highest weight and largest size
178. Ig with minimum sedimentation coefficient = IgG
179. Blood group antibodies belong to which type of immunoglobulins = IgM
180. Rheumatoid factor belongs to which type of immunoglobulins → Ig M (antibody against Fc fragment of IgG)
181. Immunoglobulin that is heat labile = IgE.
182. Ig appearing first in life = IgM
183. Ig with maximum serum concentration = IgG
184. Ig with minimum serum concentration = IgE
185. Ig with longest half-life = IgG
186. Ig with shortest half-life = IgE
187. Ig with maximum synthesis per day = IgA
188. Ig with minimum synthesis per day = IgE
189. Ig responsible for hypersensitivity pneumonitis = IgG
190. Ig to fix complements via classical pathway > IgG1 and IgM
191. Ig to fix complements via alternate pathway = IgA, IgD, IgG4
192. Warm Antibodies = Ig G, but Cold Antibodies = IgM
193. Thymus contain large no. Of lymphocytes
194. Which of the following receives sub-capsular afferents = Lymph node
195. Components of Innate immunity that are active against viral cells includes NK cells
196. Innate immunity responds best to = Carbs CHO in bacterial cell walls (LPS)
197. Associated with SLE is = DR3
198. Di George syndrome Defect in cell mediated immunity, dysfunction of = T cells occurs
199. Di George syndrome is associated with Truncus arteriosus.
200. Vaccine with best efficacy = Measles 85%
201. what is the most effective vaccine = Measles and Vaccine having maximum efficacy after single dose Measles.
202. Live virus used for active immunization against = MMR
203. Innate immunity is Fast, Nonspecific and present at Birth. Acquired immunity is specific and slow
204. Macrophages, neutrophils, and dendritic cells, which possess pattern recognition receptors (PRRs) also Called Toll like receptors for pathogen-associated molecular patterns (PAMPs) found on many Microorganisms but are absent on mammalian cell. Toll receptors are subgroup of PRR so present on above mentioned cells.
205. Natural killer (NK) cells can also detect host cells with depressed levels of major histocompatibility (MHC) class I

206.IL – 1 Acts on hypothalamus by the help of prostaglandins to cause fever Past Paper BCQ.
207.IL2 is T cell stimulator.IL3 is bone marrow regulator like CSF (colony stimulating factor (important)
208.IL4 stimulate B cell growth. Enhances class switching of IgE and IgG
209.IL5 stimulate IgA. Stimulates growth and differentiation of Eosinophils.
210.IL10 Suppress cytokine synthesis.
211.Most potent chemotactic factor for neutrophil is C5a.
212.Th1 Secrete IL-2, IFN- γ , and TNF- α and mediate cell mediated immunity
213.Th2 Secrete IL-4, IL-5, IL-10, I-13 and mediate humeral immunity
214.Th17 Secrete TGF-beta and IL-6
215.Radioallergosorbent test (RAST) is used to measure IgE in patient serum specific for a given allergen.
216.Antibodies are grouped into five classes based on differences in their heavy chains.
217.CD3 is retained on all peripheral T cells and serves as a marker for total T-cell enumeration.
218.CD34 is a marker for stem cells and permits their isolation.
219.B cells are present in follicles of white pulp
220.In D-George syndrome paracortex part of lymph node is not well developed
221.Thymus develops from 3 rd pharyngeal pouch
222.APC (Antigen presenting cells) have MHC2
223.Th1 cells are inhibited by IL – 10
224.Fc portion of IgG and IgM fixes compliment.
225.C1 esterase inhibitor deficiency leads to hereditary angioedema, ACE inhibitors are contraindicated in
226.Hereditary angioedema because they raise bradykinin levels
227.Decay accelerating factor deficiency leads to paroxysmal nocturnal haemoglobinuria. (CD 55/CD59)
228.C3b and IgG are opsonin's
229.Recurrent Neisseria bacteraemia = C4 – C9 deficiency
230.HASHIMOTO thyroiditis is = Type 4 HSR (HLA -DR5)
231.Rheumatic fever = type 2 HSR.
232.AMA antibodies done for PBC (Primary biliary cirrhosis).
233.B cells are present within follicles of white pulp. T-cells present in periarterial lymphatic sheath
234.Thymus contains capsule but no lymphatic nodule
235.Post splenectomy finding = thrombocytosis > Howell Jowell bodies
236.Definition of Graft versus host disease = immunocompetent T cells in the donor graft recognise Recipient antigens as foreign and react against them
237.Hassal corpuscles contains epithelial reticular cells.
238.Anti-basement membrane antibodies are positive in = Good Pasture syndrome
239.Fab portion is for antigen binding fragment. Fc portion is for complement binding.
240.Antigen recognized by B cells = IgG
241.Reaction after blood transfusion type 2 and during is type 1.
242.Aplastic anaemia - type 2 HSR. Aplastic anaemia along with h/o injection like Anti thymocyte globulin → type 3 HSR
243.Agammaglobulinemia is B cell disorder
244.Microtubule dysfunction and lysosomal defect = Chediak higashi syndrome
245.Anti TSH antibodies are positive in Graves' disease.
246.Aids not associated with leukaemia
247.Heparin is released by mast cells not from basophils
248.Commonest organism in transplant patient = CMV
249.Type 1 HSR release IgE. Type 2 HSR by IgG > IgM
250.Type 3= immune complex mediated. Type 4 HSR - no antibody involved
251.Patient with lung abscess and meningitis caused by = staph aureus
252.HLA DR3 is associated with graves' disease, SLE, Type 1 diabetes
253.Which antibody has memory function = IgG
254.Most abundant antibody in normal individual – IgG
255.What's the hallmark of aids = Progressive immune-depression
256.Features of type 2 hypersensitivity reaction = IgG
257.Rheumatoid arthritis is an example of = Type 3 hypersensitivity reaction
258.Antibodies present in Hashimoto thyroiditis = Antithyroglobin + anti-microsomal Ab.

259. AIDS virus is not present in = Sweat. Hep B virus is not present in stool.
260. Aids associated skin lesion = Kaposi sarcoma. Virus related to aids – EBV
261. Confirmatory test for AIDS by = Western blot
262. After giving blood transfusion, patient develops hypersensitivity reaction = Type 2 Reaction.
263. During blood transfusion Type 1 hypersensitivity-reaction
264. Lady had breast implant yrs. ago since then she is having firmness, implant fluid is leaking inside. Which cells will most likely be present = Giant cells
265. 22-year-old girls report that she was eating peanuts and began to feel itchy, developed rash over most of the body Chemical mediator for this lesion is = Mast cells
266. Cells that increase in allergic conditions are Mast cells (also basophils)
267. Cortisol decreases which of the following cells = Lymphocytes
268. Arthus reaction = Type 3 HSR
269. Regarding thymus location – Superior mediastinum
270. Aids is associated with all of following except = Primary tumour of brain
271. Earliest immunoglobulin to be synthesised by the foetus – IgM
272. At birth presence of which Immunoglobulin Indicates Intrauterine infection = IgM
273. Function of CD4 all except = Cytotoxicity
274. A child diagnosed with ITP (immune thrombocytopenic purpura). Immunoglobulin For ITP = IgG
275. Patient has aplastic anaemia, antithymocytes globulin (ATG) was given, develops allergic reaction. Type III HSR.
276. A neonate with erythroblastosis fetalis is massively transfused with whole blood, after 10 days Develops rash, first on palms, then face and trunk along with diarrhoea, what is probable cause = GVHD
277. In good pasture syndrome which type of collagen is targeted by auto antibodies = Type 4 collagen
278. Acute mild rejection of heart transplant. What will be the findings = Inc lymphocytes
279. Not HLA associated = Systemic sclerosis
280. Cells responsible for innate immunity are activated mostly by = Carbohydrate sequences in cell walls.
281. Immunoglobulin present in tears = IgA
282. In DiGeorge's syndrome which T lymphocytes are still present = Intra – epithelial lymphocytes
283. Cytologic marker useful in the diagnosis of Hodgkins lymphoma = CD15
284. Primarily B-cell marker = CD 19,20
285. An intravenous drug user has suffered from recurrent pneumonias, fungal infections in the Axillae, and a recent ear infection. He now presents with a cough and painful swallowing. Physical Examination reveals a patchy, white oral lesion. Cells with which of the following markers are most likely to be deficient in this patient = CD4
286. Systemic sclerosis Is characterised by Excessive fibrosis all over the body
287. Which of the following causes hypocalcaemia = 25 hydroxy cholecalciferol

BIOCHEMISTRY

Glycogen storage diseases (GSDs)

- At least 15 types identified but imp ones are given below.
- Main presenting features are hypoglycemia + hepatomegaly.
- Glycogen is an animal homopolysaccharide.
- It has alpha 1-4 linkages in chains & alpha 1-6 linkages in branches.
- Limit dextran:** 2-4 glucose residues left after glycogen phosphorylases cleaves glycogen.

Disease	Enzyme deficiency	Clinical Features
Type 1 Von Gierke's disease	Glucose-6 phosphatase	<ul style="list-style-type: none"> Fasting Hypoglycemia + hepatomegaly. increase Blood Lactate, TAGs, Uric Acid. Avoid Fructose and galactose. Give Oral Glucose/Corn starch.
Type 2 Pompe disease	Lysosomal Acid α 1-4 Glucosidase /Acid Maltase with α 1-6 glucosidase activity	<ul style="list-style-type: none"> Cardiomegaly, hypotonia exercise intolerance and early death Pompe thrashes Pump (Heart)
Type 3 Cori disease	Debranching Enzymes Alpha 1-6 Glucosidase + 4 α D- glucanotransferase	<ul style="list-style-type: none"> Milder than von Gierke's disease. limit dextran accumulation in blood. normal blood lactate. Gluconeogenesis is intact.
Type 4 Andersen disease	Branching Enzyme Alpha 1-4 Glucan/Glycosyl transferase	<ul style="list-style-type: none"> Hepatomegaly and hypotonia. Failure to thrive. childhood cirrhosis - early childhood death.
Type 5 McCardle's disease	Skeletal muscle Glycogen phosphorylase deficiency	<ul style="list-style-type: none"> Blood glucose unaffected. Take low carbs + high protein diet.
Type 6 Her's disease	hepatic glycogen phosphorylase deficiency	<ul style="list-style-type: none"> Hypoglycemia fatigue, and exercise intolerance

Tips to Remember GSDs

- VON = One, so it is a type 1, most Common type - 90%, also frequently asked in Exams
- Pomp = Pump, so it thrashes the Pump (Heart)
- A-B = Andersen disease – Branching enzyme deficiency
- C-D = Cori disease --Debranching enzyme def.
- M = McCardle's/ Muscle.
- H for Her's / Hepatic.

Lysosomal storage diseases

Mucopolysaccharidosis: includes Hurler and Hunter syndrome.

Sphingolipidosis: includes Tay sach's, Gaucher, Niemann pick, Fabry, and, Krabby disease.

Disease	Enzyme deficiency	Findings
Hurler syndrome	Alpha L-iduronidase (Autosomal recessive)	<ul style="list-style-type: none"> Heparin & dermatan sulphate accumulation. Corneal clouding
Hunter syndrome	Iduronate-2 sulfatase (X-linked recessive)	<ul style="list-style-type: none"> Heparin & dermatan sulphate accumulation Hunter can see (No Corneal clouding)
Tay sach's disease	Hexosaminidase A	<ul style="list-style-type: none"> Accumulation of GM2 gangliosides Cherry red spot in Macula, developmental delay No hepatosplenomegaly
Niemann Pick disease	Sphingomyelinase	<ul style="list-style-type: none"> Accumulation of Sphingomyelin Neurodegeneration, cherry red macular spot Foam cells, Hepatosplenomegaly
Gaucher disease	Glucocerebrosidase or Beta glucosidase	<ul style="list-style-type: none"> Accumulation of Glucocerebrosides Gaucher cells (Crumpled tissue papers like) Hepatosplenomegaly, avascular necrosis of femur
Krabby disease	Galactocerebrosidase	<ul style="list-style-type: none"> Accumulation of galactocerebroside. Failure to thrive, seizures, floppy to rigid tone
Fabry disease	Alpha-galactosidase A	<ul style="list-style-type: none"> Accumulation of Ceramide Tri hexose Angiokeratomas, hearing or vision affected

Lipoproteins	Type	Features	Apo-protein	Functions
	HDL	<ul style="list-style-type: none"> ○ Synthesized in Liver ○ Normal > 50 mg/dl ○ smallest size ○ Highest Lipoprotein content ○ Phospholipids -- highest amount or content. ○ A-band on electrophoresis 	<ul style="list-style-type: none"> ○ Apo A, C, D, E ○ Apo A-I is HDL receptor. 	<ul style="list-style-type: none"> ○ Transfer of Cholesterol from Periphery to Liver i.e. good cholesterol ○ Periphery → Muscles & Fat tissue.
	LDL	<ul style="list-style-type: none"> ○ Normal < 130 mg/dl ○ Synthesized in Plasma ○ Abundant in Blood ○ Highest Cholesterol content ○ Beta band on electrophoresis. 	<ul style="list-style-type: none"> ○ Apo B-100, ○ Apo C, E ○ Apo B-100 is LDL receptor 	<ul style="list-style-type: none"> ○ Transfer of Cholesterol from liver to periphery i.e. Bad cholesterol ○ Freidweld formula for LDL.
	VLDL	<ul style="list-style-type: none"> ○ Liver is the source. ○ Converts into IDL, High TAGs content, Pre-Beta Band on electrophoresis 	<ul style="list-style-type: none"> ○ Apo-B100, C, E 	<ul style="list-style-type: none"> ○ Transfer of endogenous TAGs from liver to Periphery
	CMs	<ul style="list-style-type: none"> ○ Source: GIT (Enterocytes) ○ Largest size ○ Highest TAG content ○ No Migration on electrophoresis 	<ul style="list-style-type: none"> ○ apoB-48, C1, E1, A 	<ul style="list-style-type: none"> ○ Exogenous dietary TAGs from GIT to periphery (Muscle + Adipose tissue)

*High density lipoprotein (HDL), Low density Lipoprotein (LDL)

*Very low-density lipoproteins (VLDL), Chylomicrons (CMs)

Familial Dyslipidaemias	Type	Pathogenesis & Labs	Findings
	Type I Hyperlipoproteinemia Or Familial Cylomicronemia	<ul style="list-style-type: none"> ❖ Lipoprotein Lipase deficiency (OR) ❖ Apo C-2 deficiency ❖ ↑ Cholesterol, Chylomicrons, and TAG ❖ Creamy layer in supernatant 	<ul style="list-style-type: none"> ❖ Pruritic Xanthomas ❖ No risk of Atheroma
	Type II Hyperlipoproteinemia Or Familial Hypercholesterolemia	<ul style="list-style-type: none"> ❖ Most common in children ❖ Absent/defective LDL receptor or defective Apo B-100. ❖ Type IIa: ↑ LDL, cholesterol ❖ Type IIb: ↑ LDL, cholesterol, VLDL 	<ul style="list-style-type: none"> ❖ Achilles Xanthomas ❖ Corneal Arcus ❖ Accelerated Atheroma ❖ May have MI < 20 yrs old. ❖ Cholesterol 300- 700 mg/dl
	Type III Dysbetalipoproteinemia	<ul style="list-style-type: none"> ❖ Apo-E (Three has Es) ❖ ↑ Chylomicrons + VLDL (TAG) 	<ul style="list-style-type: none"> ❖ Palmar xanthomas ❖ palm is supplied by 3 nerves. ❖ palmar xanthoma-Type III
	Type IV Hypertriglyceridemia Or Familial Hyperlipidemia	<ul style="list-style-type: none"> ❖ Most common in adults + overall ❖ Hepatic VLDL Over production ❖ ↑ VLDL + TAGs 	<ul style="list-style-type: none"> ❖ Acute Pancreatitis ❖ TAGs can be > 1000mg/dl. ❖ Insulin Resistance present
	Type V Endogenous Hypertriglyceridemia	<ul style="list-style-type: none"> ❖ Type V= Type IV + Type I ❖ ↑ VLDL, ↓ Lipoprotein Lipase ❖ Inc VLDL + chylomicrons in blood 	<ul style="list-style-type: none"> ❖ Hepatosplenomegaly ❖ pancreatitis.

KEY FACTS	
Normal total cholesterol : less than 200 mg/dl, 200 – 240 – borderline, > 240 cholesterol - high level	
lipoproteins with highest TAG content → chylomicrons (highest) > CM remnant > VLDL > LDL > HDL (lowest)	
lipoproteins with highest protein or phospholipids content → HDL > LDL > VLDL > chylomicrons (Lowest)	
lipoproteins with highest cholesterol content → LDL > VLDL > HDL > chylomicrons	
Best predictor of future MI: CRP (highly sensitive) > TC/HDL ratio > Apo b/Apo a ratio > LDL > non-HDL (TC - HDL) > HDL HDL is negative coronary risk factor and LDL Or lipoprotein a is +ve risk factor for IHD	
Type I & IV Hyperlipidemia = autosomal recessive whereas type II + type III = autosomal dominant	
Type I → pruritic xanthomas; type II → Achilles xanthomas; type III → palmar xanthomas	
T for tendons and two. so, tendons/Achilles xanthomas in type II. Apo C-2 activates LPL normally	
inc TAGs are linked to acute pancreatitis	
Abetalipoproteinemia: Mutation in gene for Microsomal Transfer Protein (MTP). Def of ApoB48, ApoB100. Leads to absence of VLDL & LDL. Acanthocytes on smear and Lipid Laden Macrophages on intestinal Biopsy. Features include Steatorrhea, Failure to thrive & later Ataxia, Spinocerebellar degeneration. Treat with Oral Vit E + Restriction of Long chain Fatty Acids.	

Anti-Hyperlipidemic drugs	Drug Group	Mechanism	
	Statins	Atorvastatin , rosuvastatin Reduce cholesterol synthesis in Liver by inhibiting HMG CoA Reductase	
	Fibrates	Clofibrate , gemfibrozil inc Lipoprotein lipase activity in blood and break VLDL from TAGs	
	Bile acid binding resins	Cholestyramine, colestipol act in the gut to reduce fat absorption	
	Niacin	acts on liver to dec VLDL secretions. side effects include Hyperuricemia and hyperglycaemia	
	Ezetimibe	decrease cholesterol absorption from gut	
Key Facts	Drugs that Best Raise HDL : Niacin > Fibrates > statins > Fish Oil		
	Best Lower LDL (Bad Cholesterol) : Statins > Ezetimibe > Bile acid resins > Niacin		
	Main side effect of statins is Rhabdomyolysis & hepatotoxicity.		
	Never give statins in pregnancy		
	Best Lower TAGs: Fibrates > Niacin > statins		
	S/ E of Fibrates include GIT distress/ Flatulence.		
	Bile acid sequestrants may cause Gall stones.		
	Avoid Anti Hyperlipidemic (Hypolipidemic) drugs in: Liver dysfunction, Pregnancy, Biliary diseases, and Gall stones		

VITAMINS				
Fat soluble vitamins	Vit A, D, E, K They are stored in body and required (in weeks). May cause hypervitaminosis or toxicity.			
	<table> <tr> <th>Vitamin</th><th>Description</th></tr> <tr> <td>Vit A</td><td> <ul style="list-style-type: none"> ➤ Plants source: Retinol while from Animal source: Retinal ➤ Source: Carrots – Beta carotenes, Potatoes, Liver, fish, and egg. ➤ Recommended dose is 5000 IU. ➤ Essential for Differentiation of epithelium, Prevents Squamous Metaplasia ➤ Antioxidant + Required for vision. ➤ Used in Measles and AML; M3 (All trans retinoic acid is used) ➤ Night Blindness an earliest symptom/manifestation of deficiency ➤ Corneal xerosis is the earliest sign, ➤ Other signs are Bitot spots, dry skin, dry eyes spots, keratomalacia. ➤ Paraffin use can cause Vit A deficiency. ➤ Hypervitaminosis A leads to Scaly dermatitis > Jaundice or hepatomegaly. ➤ other features of excess are Alopecia, Raised ICP, idiopathic Intracranial HTN </td></tr> </table>	Vitamin	Description	Vit A
Vitamin	Description			
Vit A	<ul style="list-style-type: none"> ➤ Plants source: Retinol while from Animal source: Retinal ➤ Source: Carrots – Beta carotenes, Potatoes, Liver, fish, and egg. ➤ Recommended dose is 5000 IU. ➤ Essential for Differentiation of epithelium, Prevents Squamous Metaplasia ➤ Antioxidant + Required for vision. ➤ Used in Measles and AML; M3 (All trans retinoic acid is used) ➤ Night Blindness an earliest symptom/manifestation of deficiency ➤ Corneal xerosis is the earliest sign, ➤ Other signs are Bitot spots, dry skin, dry eyes spots, keratomalacia. ➤ Paraffin use can cause Vit A deficiency. ➤ Hypervitaminosis A leads to Scaly dermatitis > Jaundice or hepatomegaly. ➤ other features of excess are Alopecia, Raised ICP, idiopathic Intracranial HTN 			

		<ul style="list-style-type: none"> ➤ Prefer scaly dermatitis or dry skin. ➤ Isotretinoin is a Teratogenic that may cause NTDs and Cleft palate
	Vit D	<ul style="list-style-type: none"> ➤ Vit-D (Cholecalciferol), D3 (in milk, also formed in skin) Ergocalciferol (D2-Plants) ➤ Cod Liver Oil is the richest source of Vit D other sources are Eggs, milk, Sunlight. ➤ Storage Form: 25-OH D3 (Liver) ➤ in Liver : 25-hydroxylation while in kidney: Alpha-1 hydroxylation ➤ Give Oral Vit D to Breastfed infants as it is Not present in breast milk. ➤ Main effects are on Calcium + Bones: Inc GIT absorption of Both Ca + PO₄. ➤ At low levels Increase Mineralization while at high levels increase Bone Resorption ➤ Deficiency: leads to Rickets in children and Osteomalacia in adults, Tetany, Hypocalcaemia, Hypophosphatemia, Chvostek sign +Trousseau's sign for low Ca²⁺ ➤ Excess causes Hypercalcemia, Hypercalciuria, Stupor, Loss of appetite ➤ Excess may be seen in granulomatous diseases (Sarcoidosis) ➤ Recommended dose for Infant & Child: 400 IU, Adults: 400-600 IU, Pregnant & Breast Feeding: 600 IU, Old age: 800 IU
	Vit E	<ul style="list-style-type: none"> ➤ Vit E (Tocopherol) Sources are Nuts, seeds, avocado, Whole grains. ➤ Strongest Antioxidant vitamin ➤ Protect RBCs & Germinal epithelium from free Radicals injury. ➤ Deficiency causes: Hemolytic anemia, Muscular Weakness, Demyelination of Posterior Columns ➤ (Same as Vit B12 def, but no Megaloblastic anemia) ➤ Risk of Enterocolitis in infants due to excess Vit E ➤ It Increase the effect of warfarin Or Warfarin toxicity
	Vit K	<ul style="list-style-type: none"> ➤ Plants: Phylloquinone K1 and in Animals: Menaquinone K2 ➤ Source: Green leafy Vegetables (Broccoli & Brussels) ➤ Synthesized by Intestinal Flora. Not found in Breast Milk. Required for Coagulation ➤ Synthesis of clotting factors 2,7,9,10, and Protein C & S ➤ Give vit K injection, IM 1mg/0.5mL to all New-borns because Gut is sterile at Birth. ➤ Deficiency causes Haemorrhage (neonatal) With raised PT, APTT, but normal BT. ➤ Prolonged use of Broad-spectrum antibiotics also Causes def of Vit K ➤ Excess may lead to Jaundice. Recommended Dose / RDA = 80 ug
Water soluble vitamins	Vit B complex & c. They are not stored in body (except b12) so, frequently required (daily).	
	Vitamin	Description
	Vit C Ascorbic Acid	<ul style="list-style-type: none"> ➤ Source: citrus fruits +Vegetables e.g. Orange, Lemon, kiwi, Strawberry. ➤ Required by Dopamine Beta hydroxylase to convert Dopamine to NE. ➤ Antioxidant, ↑ Fe absorption. ➤ Vit C is Hydroxylation of lysine & Proline for Collagen synthesis. ➤ Used in Treatment of Methemoglobinemia converts Fe³⁺ to Fe²⁺. ➤ Deficiency causes Scurvy, weak immunity, poor wound healing, and hemolytic anemia. ➤ Deficiency increases by Tea & Toast diet. ➤ SCURVY: swollen gums, petechiae, easy bruising, Hemolytic anemia, poor wound healing, Perifollicular & Sub periosteal Hemorrhages, Hemopericardium. ➤ Excess may cause Ca-Oxalate Stones, Worsens Hemochromatosis by increase Fe toxicity, Diarrhoea, Nausea, Vomiting, fatigue. ➤ RDA: 60mg while max dose per day can be 2000mg.
	Vit B1 Thiamine	<ul style="list-style-type: none"> ➤ Vit- B1 (Thiamine –TPP) Source: Rice, Beans, Lentils, Peas, Enriched Cereals, Wheat ➤ Processing/Boiling of Rice Removes Thiamine from Rice. ➤ Par-Boiling Preserves Vit B1 ➤ Required For Carbs Metabolism as It Is in Thiamine Pyrophosphate (TPP) A Cofactor For → Dehydrogenases Branched Chain Keto Dehydrogenase, Alpha KG (TCA Cycle), Pyruvate Dehydrogenase (Links Glycolysis To TCA), Transketolase (HMP Shunt) ➤ Imp For Good Memory B1 > B3 ➤ Vit B1 Def Effects Heart & Brain. ➤ Dry Beri- Beri = Polyneuropathy, Muscle Wasting

	<ul style="list-style-type: none"> Wet Beri-Beri Causes High Output HF Wernicke-Korsakoff Syndrome: Necrosis of Mammillary Bodies + Medial Dorsal Thalamic Nuclei in Chronic Alcoholics Leading to Memory Loss (Permanent). Amnesia Of Both Types Seen but Anterograde > Retrograde. B1 Def Diagnosed by Increased RBC Transketolase Activity Following B1 Administration RDA: 1.5mg <p>Key Facts:</p> <ul style="list-style-type: none"> High Output Cardiac Failure Caused By = Beri-Beri > Thyrotoxicosis > Anemia B1 Required for Good Memory. B1 Def Causes CNS Dysfunction. B1 Present in Wheat + Rice.
Vit B2 Riboflavin	<ul style="list-style-type: none"> Vit-B2 (Riboflavin) Source: Milk, yogurt, Cheese, eggs, lean meat Important for Proteins metabolism as a component of FMN, FAD in Redox reactions e.g., in TCA cycle Def leads to Corneal Vascularization, Cheilosis and Magenta Tongue (Purple) RDA: 1.7mg Remember; FMN&FAD generate 2ATPs, (So B2 for FMN, FAD)
Vit B3 Niacin	<ul style="list-style-type: none"> Vit-B3 (Niacin/ Nicotinamide) Source: Turkey breast, chicken Breast, tuna fish Maize is rich source of B3. B3 is Derived from Tryptophan. B3 Synthesis requires Vit B2+ B6. Niacin is Constituent of NAD+ & NADP and treats Dyslipidaemias. It Raises HDL but it Decreases VLDL. Deficiency leads to Pellagra: 4 Ds → Diarrhea, Dementia, Dermatitis (Collar rash or Necklace rash with C3/C4 involvement) and Death. Other causes of Niacin def are: Hartnup disease-abnormal tryptophan metabolism and Carcinoid syndrome. RDA: 20mg. Excess Niacin may cause GOUT, Hyperglycemia, Flushing/itching
Vit B5 Pantothenic Acid	<ul style="list-style-type: none"> Vit-B5 (Pantothenic acid) Source: egg, beef, salmon Component of: Coenzyme A (CoA) and fatty acid synthase Def may cause Adrenal insufficiency (burning hands & Feet), Dermatitis, Alopecia RDA: 10mg
Vit B6 Pyridoxine	<ul style="list-style-type: none"> Vit B6 (Pyridoxine) Source: Peanut, chicken, soya beans, Oat B6 Converted into Pyridoxal phosphate (PLP) that is used in Transamination (ALT/AST) reactions, Decarboxylation, and glycogen phosphorylase. B6 is Used in the synthesis of: Heme, histamine, Niacin Glutathione, Cystathionine Serotonin, GABA, DOPA, NE & Epinephrine. Deficiency occurs mostly in Dialysis patients. Def causes Peripheral Neuropathy: induced by Isoniazid + OCPs, Sideroblastic anemia and Seizures. RDA = 6mcg
Vit B7 Biotin	<ul style="list-style-type: none"> Vit-B7 (Vit H/BIOTIN) Source : Nuts eggs, meat, avocados Cofactor for Carboxylation reactions: Acetyl CoA carboxylase, Pyruvate Carboxylase Imp for Fat metabolism biotin is a Carrier Of 1-Carbon or adds 1- (C) fragments. Ingestion of Raw eggs 20/day; avidin in egg white leads to B7 def. Diarrhea and Alopecia rarely occurs. Long term antibiotics usage may cause B7 def also. RDA: 30ug
Vit B9 Folate	<ul style="list-style-type: none"> Vit B9 (Folate/Folic acid) Source : Green leafy vegetables, Spinach, Turnip, Brussels Folate is Stored in Liver for 3-4 Months Most common type of megaloblastic anemia is folic acid deficiency. Absorbed in JEJENUM. Imp for DNA+RNA synthesis by formation of Nitrogenous bases B9 converts into THF -tetrahydrofolate - active form and acts as Coenzyme for 1-Carbon transfer, not addition of 1-Carbon

		<ul style="list-style-type: none"> ✚ Drugs that dec folate: Phenytoin, Sulphonamides, and methotrexate ✚ Goat Milk has low folate -- children who consume it are at risk of folate deficiency. ✚ Diet dependency on fast foods like burger increases the risk of folate deficiency. ✚ Anemia of Macrocytic Hypochromic type occurs in folate def. ✚ Megaloblastic anemia with Hypersegmented Neutrophils. No neurological signs ✚ Folate deficiency → Neural tube defects e.g., Spina bifida . ✚ Diagnosis: RBC folate levels are confirmatory ✚ Raised Homocysteine levels and Normal Methyl malonic acid. ✚ Start Folic acid 1 month prior to conception and continue in whole Pregnancy. ✚ Dose: 400 mcg daily in pregnancy to avoid NTDs.
	Vit B12 Cobalamin	<ul style="list-style-type: none"> ✚ Vit-B12 (Cobalamin) Cyanocobalamin or Methycobalamine. ✚ Animal source Only: Meat, Poultry, eggs. ✚ Storage: 3-4 yrs. in Liver ✚ B12 Synthesized only by Microorganisms. RDA: 8ug ✚ Absorption: Terminal Ileum ✚ B12 is Imp for DNA synthesis. ✚ Cofactor for methionine Synthase + methyl malonyl CoA mutase ✚ Red Beefy Tongue in B12 def. ✚ Causes of b12 deficiency: ✚ Diphyllbothrium Latum (fish tapeworm), Veganism or strict Vegetarian diet. ✚ Drugs: Like metformin and Omeprazole -- that cause achlorhydria. ✚ Bacterial Overgrowth ✚ Lack of Intrinsic. Factor e.g., in pernicious Anemia dec b12 ✚ Features of B12 def: ✚ Megaloblastic anemia -- Hypersegmented PMNs (neutrophils). ✚ Neurological signs: paraesthesia, Numbness, Ataxia, and gait abnormalities ✚ Diagnosis of B12 deficiency: Serum B12 levels ✚ Raised Methyl Malonyl CoA & homocysteine levels in B12 def. ✚ Folic acid supplementation can reverse the haematological abnormalities but can't reverse the neurological abnormalities of b12 def.
	Key Facts	<ul style="list-style-type: none"> ❖ Vit B1 is essential for Carbohydrates metabolism. ❖ Vit B2 is important for Proteins. ❖ Vit B7 is required for Fats metabolism. ❖ For Good Memory: Vit B1 > B3 ❖ Peripheral Neuritis / Neuropathy: vit B1 > Vit B6 > vit B12 ❖ Optic Neuritis: B12 > B6 ❖ Best Antioxidants: Glutathione >Transferrin > Vit E > Vit C > Vit A ❖ Zinc deficiency causes Azoospermia, dysgeusia, anosmia, and acrodermatitis enteropathy. ❖ Chronic Pancreatitis causes Steatorrhea which leads to Fat sol vit def. ❖ Folic acid transfers 1-Carbon; whereas Biotin carries or Adds 1- Carbon

CLASSIFICATION OF AMINO ACIDS (AA)		
Based on Polarity	<ul style="list-style-type: none"> Hydrophilic (polar) and Hydrophobic (non-polar). Only L type amino acids are present in proteins. 	
Based on chemical nature	Acidic AA (-Ve charge)	<ul style="list-style-type: none"> Aspartic acid, asparagine, glutamic acid, glutamine
	Basic AA (+Ve charge)	<ul style="list-style-type: none"> Histidine, arginine, lysine. Arg is the most basic amino acid. Arg and Histidine are required for active growth. Arg and Lys are in Histone which bind the DNA.
	Aromatic	<ul style="list-style-type: none"> Phenylalanine, tyrosine, tryptophan
	Sulphur containing	<ul style="list-style-type: none"> Cysteine, methionine
	OH-containing	<ul style="list-style-type: none"> Serine, threonine
	Imino acid	<ul style="list-style-type: none"> proline
	Aliphatic side chain	<ul style="list-style-type: none"> Glycine, alanine, valine, leucine, isoleucine
Based on Metabolic fate	Glucogenic	<ul style="list-style-type: none"> Alanine, glycine + all other AAs except given below. Gluconeogenesis depends upon availability of Alanine in blood
	Ketogenic	<ul style="list-style-type: none"> Lysine, leucine
	Both gluconeogenic and ketogenic	<ul style="list-style-type: none"> Phenylalanine, isoleucine, tyrosine, tryptophan (PITT)
Nutritional classification	Essential AA (10)	PVT TIM HALL = Phenylalanine, valine, tryptophan, threonine, isoleucine, methionine, histidine, arginine, leucine, lysine
	Non-essential	Tyrosine, Glycine, alanine, serine, cysteine, aspartate, glutamate, glutamine, proline
	Semi-essential	Histidine, arginine
KEY FACTS	<ul style="list-style-type: none"> Amino acid deficiency causing injury to cell is Glycine (protects cell membrane) Amino acid in excess causes injury to cell is Choline. Inability to convert glycine into glyoxalate may cause renal stone. Histamine is not AA, but it is amino peptide. Amino acid in abnormal metabolism is Tryptophan – Hartnup disease. amino grp source in urea cycle is aspartate + glutamate. Nitrogen source in urea cycle is aspartate + ammonia. Urea cycle occurs in liver. 	
Amino Acid	Derivatives	
Tyrosine	<ul style="list-style-type: none"> Thyroxine, melanin, Dopamine, nor epinephrine, epinephrine 	
Tryptophan	<ul style="list-style-type: none"> Niacin, serotonin (melatonin is serotonin derivative) 	
Glycine	<ul style="list-style-type: none"> Heme Glycine + cysteine → bile salts Glycine + arginine + methionine → Creatinine Glycine + glutamic and aspartic acid → Purine bases 	
Glutamic acid	<ul style="list-style-type: none"> GABA, glutamic + aspartic acid → pyrimidine bases 	
Alanine	<ul style="list-style-type: none"> Coenzyme A 	
Histidine	<ul style="list-style-type: none"> Histamine (an amino peptide, not amino acid) 	

DISORDERS OF PROTEIN METABOLISM (CATABOLISM)		
Disorder	Defective Enzyme & Process	Features
Phenylketonuria (PKU) (AR)	<ul style="list-style-type: none"> Inability to convert phenylalanine to tyrosine due to Phenylalanine hydroxylase deficiency. Most common congenital metabolic disorder Treated with low phenylalanine but high tyrosine diet. Tyrosine becomes essential Amino acid here. 	<ul style="list-style-type: none"> Neonatal vomiting and mental retardation Musty body odour due to phenylacetate, phenylpyruvate and phenylacetate accumulation in blood Screening occurs 2 -3 days after birth (normal at birth) due to maternal enzyme during fetal life. Maternal PKU: due to ↑ maternal phenylalanine levels, prevented by decreased dietary intake.

Alkaptonuria	<ul style="list-style-type: none"> Homogentisic acid oxidase deficiency Defective tyrosine degradation 	<ul style="list-style-type: none"> Black discoloration of urine, joints, or articular cartilage i.e., Ochronosis
Maple syrup urine disease	<ul style="list-style-type: none"> Def of branch chain alpha keto dehydrogenase, accumulation of isoleucine, leucine & valine 	<ul style="list-style-type: none"> Smell of burnt sugar in urine, vomiting, seizures, mental retardation, and early death. Thiamine supplements are helpful
Albinism	<ul style="list-style-type: none"> Def of tyrosinase, defective melanin synthesis from tyrosine 	<ul style="list-style-type: none"> Lack of pigmentation in skin, eyes, hair
Cystinuria	<ul style="list-style-type: none"> Defect in renal and GIT transporter for COLA: Cysteine, Ornithine, lysine, and arginine 	<ul style="list-style-type: none"> Renal stone, abnormal urine nitroprusside test
Homocystinuria	<ul style="list-style-type: none"> Cystathionine beta synthase def. Defective methionine degradation 	<ul style="list-style-type: none"> Mental retardation (low IQ), Lens dislocation Bone developmental defect
Carbomyl phosphate synthetase 1 def.	<ul style="list-style-type: none"> Deficiency of Carbomyl phosphate synthetase 1 	<ul style="list-style-type: none"> Lethargy, seizures, and early death

Hyperammonia	<ul style="list-style-type: none"> ❖ caused by CLD/Urea cycle defects. ❖ it leads to ↑ Glutamine Induced Osmotic damage, ↓ GABA & Alpha KG. ❖ Presents with Slurred speech, asterixis, somnolence. ❖ Treat with Rifaximin + lactulose + Limitation of Proteins ❖ Ornithine Transcarboxylase def is the Most common Urea cycle disorder that presents with Orotic aciduria and ↑ serum NH₃ levels
Cori Cycle	<ul style="list-style-type: none"> ❖ Uses lactate from skeletal muscle + RBCs to generate glucose. ❖ It involves the shuttling of lactate from red blood cells and muscle to the liver to be used as a substrate for gluconeogenesis and it Produces 4 ATPs

IMPORTANT ENZYMES FOR METABOLISM

Kinase	Catalyses transfer of a phosphate group from a high-energy molecule (usually ATP) to a substrate. While Transferase transfers groups like OH, acyl & methyl etc.
Phosphorylase	Adds inorganic phosphates onto substrate without using ATP.
Phosphatase	Removes phosphate group from substrate.
Dehydrogenase	catalyses oxidation-reduction reactions (e.g pyruvate dehydrogenase)
Hydroxylase	Adds hydroxyl group (-OH) onto substrate (e.g tyrosine hydroxylase).
Carboxylase	Transfers CO groups with the help of biotin (e.g, pyruvate carboxylase)
Mutase	Relocates a functional group within a molecule.
Synthetase	Synthase or synthetase Joins two molecules together using a source of energy (ATP acetyl-CoA)
Hepatic lipase	Degrades TAGs remaining in IDL and chylomicron remnants.
Hormone sensitive lipase	Degrades TAGs stored in adipocytes. Promotes Gluconeogenesis by releasing glycerol.
Lipoprotein lipase	Degrades TAGs in circulating chylomicrons.
Pancreatic lipase	Degrades dietary TGs in small intestine.
Lecithin-cholesterol Acyltransferase	catalyses esterification of plasma cholesterol (required for HDL maturation)

Carrier Molecule	Carried in activated form
ATP	Phosphoryl groups
Biotin	CO₂ (carrier/ adds 1-Carbon)
Tetrahydrofolate(B9)	1-Carbon Units transfer
S-Adenosyl methionine (SAM)	Methyl group (CH ₃)
NADPH, FADH ₂	Electrons

- ❖ Universal Electrons Acceptors are NAD, NADP (from B3), FAD (from B2)
- ❖ NAD is used In Catabolic reactions whereas NADPH is used in Anabolic reactions.
- ❖ NADPH Is Product of HMP Shunt.
- ❖ It is used in Respiratory Burst, Cytochrome P-450 System, and, Glutathione Reduction

Pentose phosphate pathway or HMP Shunt	<ul style="list-style-type: none"> It Provides NADPH and additionally Ribose. NO ATP production. HMP shunt Occurs in RBCs, Liver, adrenal cortex, Lactating Breasts. Protects RBCs from Oxidative damage. G6PD Is rate Limiting enzyme in this pathway. Its def causes hemolytic anemia
G6PD deficiency	<ul style="list-style-type: none"> X linked Recessive disease that causes self-Limited hemolysis due to dec NADPH required for RBCs survival against oxidizing agents. Triggers: most common is Infection > Drugs (Primaquine, Dapsone, Sulfonamides) > Fava Beans. G6PD def produces Heinz bodies (precipitated Globin chains) and Bite cells

Insulin Vs Glucagon

- Insulin causes Storage of glycogen, Lipids & proteins. Activates LPL [↑] TAGs but inactivates HSL enzyme.
- Glucagon + Epinephrine cause Use of Fuel Reserves (glycogen, free fatty acid+ Amino Acids)

Fasting Vs Starvation	Aim is to supply Glucose to Brain + RBCs and Preserve Protein
Fed State	(After Meal): Glycolysis +Aerobic Respiration Provides Energy. (BCQ)
Fasting	B/w meals - Hepatic Glycogenolysis > Hepatic Gluconeogenesis provides energy. Free fatty acids are minors source

KEY FACTS - STARVATION

order of utility of resources: carbohydrates (glycogen) > lipids > proteins (amino acids).	
glycogen reserves deplete by day 1 (RBCs can't use ketones as they lack mitochondria)	
after 48hrs: free fatty acids (FFAs) become main source of energy.	
after 3 days: vital protein degradation starts (amino acids are utilized now).	
brain uses ketone bodies. especially (beta hydroxy butyrate). acetone present in blood (fruity odour)	
amino acids provide best substrate for gluconeogenesis	
gluconeogenesis depends upon supply of alanine in the blood.	
SITES OF METABOLISM	
Cytoplasm	Glycolysis, HMP Shunt, Syntheses of: Fats, Cholesterol Proteins and Nucleotides.
Mitochondria	TCA cycle , ketogenesis, Beta-Oxidation of Fatty acids, Oxidative Phosphorylation, Alcohol
Both Cytoplasm + mitochondria	Gluconeogenesis, Heme synthesis, Urea cycle
ATP PRODUCTION IN INTENSE EXERCISE	
First 10 sec	Phosphocreatine Shuttle by enzyme Creatine kinase It is the Quickest/Fastest source.
10 – 60 sec	anaerobic glycolysis, increase Lactic acid
60 sec	Oxidative Phosphorylation ; Slowest but most effective

ETHANOL METABOLISM

- Ethanol increases **NADH/NAD⁺** ratio in **Liver** and causes these effects.
 - Lactic acidosis** (increase Pyruvate conversion to Lactate).
 - Ketoacidosis** (diversion of **acetyl CoA** into Ketosis)
 - Fasting Hypoglycemia (By Dec Gluconeogenesis)
 - Hepatosteatorsis** (acetyl coA diverts to Fatty acids)
- It follows **Zero Order Kinetics**. **NAD⁺** is the Limiting Reagent.
- Females are More Susceptible to ethanol Poisoning due to **↓** activity of **Gastric Alcohol Dehydrogenase**, dec Body Size and decrease water % in body.

Fomepizole	<ul style="list-style-type: none"> Blocks Alcohol Dehydrogenase. Antidote for Methanol poisoning. Ethanol can also be used for Methanol Overdoses. Blindness occurs in Methanol Poisoning
Disulfiram	<ul style="list-style-type: none"> It Blocks Acetaldehyde Dehydrogenase and Discourages drinking by increase Hangover symptoms like Flushing, Headache due to ↑ Acetaldehyde levels (BCQ)

Hexokinase	<ul style="list-style-type: none"> ❖ Low Km and Vmax, Present in All tissues except Liver and Pancreas ❖ Sequesters Glucose in tissues even when Glucose is Low. ❖ Feedback inhibition by Glucose-6Phosphate
Glucokinase	<ul style="list-style-type: none"> ❖ High and Vmax, present in Only Liver & Pancreas (Beta cells) ❖ Helps in Storing Glucose in Liver at higher glucose levels. ❖ Inhibited by Fructose-6 Phosphate
Glucose-6 phosphatase	<ul style="list-style-type: none"> ❖ Present in Liver (Smooth ER), kidney & GIT. Absent in Muscle *(BCQ) ❖ Maintains Euglycemia during fasting by Gluconeogenesis. ❖ Muscles can't do Gluconeogenesis as Glu-6 P is Absent ❖ NO increase in Serum Glucose even after Giving Fructose indicates Glucose-6 Phosphatase deficiency

KEY FACTS - CARBS METABOLISM

- 1 molecule of glucose broken down into water+CO₂ gives Total 38 ATP: but Net ATP is 32.
- Aerobic Metabolism: via Malate aspartate shuttle (Heart& Liver) gives net 32 ATP
- Glycerol 3-Phosphate shuttle (Skeletal Muscles) gives Net 30 ATPs
- Anaerobic Metabolism yields Net 2 ATPs. Arsenic poisoning causes glycolysis to give Zero ATP
- Deficiency of Glucokinase Is Associated with Maturity onset Diabetes & Gestational DM
- Same Substrate for Glycolysis, Gluconeogenesis and HMP Shunt is **Fructose-6 Phosphate**
- Common in Glycolysis & Gluconeogenesis: **Fructose6-P** **↔** **Fructose 1-6 bisphosphate**
- **End Product of Carbohydrate Digestion is Glucose, but end product of Carbs Metabolism is Pyruvate**
- Glycolysis Yields **2 Pyruvate** molecules. To fully Metabolize glucose; TCA cycle Runs twice.
- **Cellular Respiration** yields net **36- ATPs**.
- **TCA cycle gives Net 10 ATPs/ cycle**. But total 12 ATP/ cycle are produced.
- **Electron transport Chain** can give **34 ATPs**. **Complex I of ETC (NADH)**; complex II-FADH₂
- **Complex III-Coenzyme Q**, **Complex IV (Cytochrome C)**; **Complex-V—ATP synthase**
- Remember that; **Cyanide + Carbon monoxide** block **Complex-IV of ETC**
- **Creatinine Phosphokinase (CPK) is Absent in Liver while Glu-6phosphatase absent in Muscle**.
- **Pyruvic Acid** is intermediate in Glucose to **Acetyl CoA** conversion.
- Product of **Glycolysis (ANAEROBIC type)** in RBCs is **LACTATE (LDH involved)**.
- **Acetyl CoA** can be converted to **fatty acids, Ketones & Cholesterol** except **Glucose**.
- **Irreversible** step in Glycolysis: **Fructose 6-P to Fructose1-6bisphosphate**
- Oxidation of **Odd chain FA** produces **Propionyl CoA**; Odd chains can't be used in Gluconeogenesis .
- **1 NADPH** gives **2.5 ATPs (approx. 3)**; **1FAD** gives **1.5 ATP** (2 ATP approx.).
- **Humans can Survive without Carbs or Can tolerate lack of CARBS but cannot survive without lipids**.
- Non-essential Amino Acids take **Alpha grp** from **Glutamine > Glutamate**.
- **↑ NADH/NAD⁺ ratio inhibits TCA/Krebs cycle**. Ethanol inc NADH/NAD⁺ ratio.
- **PYRUVATE DEHYDROGENASE COMPLEX**: Contains **3 enzymes & 5 cofactors** (Vit B1, B2, B3, B5 + lipoic acid)





















- **PDH** causes transition from **glycolysis to TCA/Krebs cycle**.
- **PDH def** causes build up of **pyruvate** that gets converted to **Lactate (via LDH)** and **Alanine via ALT**. Managed by inc intake of **Ketogenic diet (high Fats content)** or inc **Lysine + leucine**.
- **Lactic acidosis**: end product of Anaerobic glycolysis, occurs via LDH enzyme in RBCs, WBCs, Lens, Cornea, Testes and Renal medulla.
- **Essential Fructosuria**: Fructokinase deficiency, asymptomatic so no management required.
- **Hereditary Fructose intolerance**: Aldolase B def, Hepatomegaly, Hypoglycemia, Jaundice, avoid sucrose.
- **Galactokinase** def may cause cataract.
- **Galactosemia**: Galactose 1-P Uridyl Transferase deficient, **Cataract**, Jaundice, Hepatomegaly, and growth retardation.
- **Lactose intolerance**: def of lactase secreted by intestinal brush border presents with osmotic diarrhea.












RATE LIMITING ENZYMES

➤ Glycolysis : Phosphofructokinase-1
➤ Glycogenesis : Glycogen synthetase (Dephosphorylated form)
➤ Glycogenolysis : Phosphorylase (Phosphorylated)
➤ Gluconeogenesis : Pyruvate carboxylase and Phosphoenolpyruvate carboxykinase (PEP-C)
➤ TCA cycle : Isocitrate dehydrogenase
➤ HMP shunt : Glucose-6-phosphate dehydrogenase
➤ Urea Synthesis : CPS-I Carbamoyl phosphate synthetase, Or, Ornithine transcarboxylase
➤ Fatty acid synthesis : Acetyl CoA carboxylase
➤ Cholesterol synthesis : HMG CoA reductase
➤ Ketone bodies Synthesis : HMG CoA synthetase
➤ Fatty acid oxidation : Carnitine acyltransferase
➤ Purine synthesis : Phosphoribosyl pyrophosphate synthetase (PRPP synthetase)
➤ Uric acid synthesis : Xanthine oxidase
➤ Porphyrin synthesis : d-ALA synthetase
➤ Bile acid synthesis : 7- α -hydroxylase

NUTRITION

- **Daily Energy Requirement for an adult: 25-30 KCAL/Kg/day**
- **Serum Albumin** is **Reliable indicator** of **Nutritional status** of the Individual.

Basal metabolic rate	 Minimum energy required for life functioning.  It depends upon Lean Body Mass .  Calculated by Heat produced/body Surface area.  Normal is 37-40kcal/hr/sq. metre
Daily caloric requirement	 Adult Male: 2000 Cal/day  Adult Female: 1600 Cal/day  1g Carb/ Proteins yields = 4kcal  1g Fat= 9kcal.  1gm alcohol= 7kcal
Daily macronutrients requirements	 CARBS: 60-65% of diet or 330g-360g/day  Fats: 25-35% Of diet. Or 56gm/day  Proteins: 10-15% of diet. Or 44 to 78g/day or 1g/kg/day
Fe, Folate, Ca requirement	 Total body iron stores are 4gm. In Males 6g: Females—2g  Iron required in pregnancy is 800mg-1000mg. Prefer 800mg.  Ca required in pregnancy is 1200 mg.  Folic acid required is 400mcg (0.4ug)/day.  Take Iron with Citrus Fruits. Or 1hr before/2hr after Meal  Iron decreases Absorption of Ca ²⁺ .  So, it is advisable to take Iron at Night & Ca ²⁺ at daytime.  Tetracyclines are Ca ²⁺ chelators. So, they interfere with Ca absorption.

	 Green Leafy vegetables are good source of Folate > Calcium.  Iron richest sources are Meat, Poultry/Sea foods.  for Ca+2 -- Milk, green Vegetable, Cheeses				
Total parenteral nutrition	 Decreases risk of enteral infections.  But it increases the risk of CVP infection—most common.  Complications: infection-common; Hyperglycemia/Hypoglycemia, Vitamins  Micronutrients deficiencies:  Zn def and Essential fatty acid i.e., Linoleic acid def (can lead to Scaly Skin)  Contraindications: Uncontrolled DM > Liver Failure > DM				
Common Fatty liver cause	In Pakistan.  Starvation/Protein deprivation/Malnutrition > Obesity Worldwide  Obesity and Fatty Diet				
WHO classification of Weight status	Weight status	Body mass index (BMI) Kg/m2			
	Under weight	< 18.5			
	Normal range	18.5 – 24.9			
	Overweight	25 – 29.9			
	Obese	≥30			
	Obese class I	30 – 34.9			
	Obese class II	35-39.9			
Assessment of nutritional status	Gomez Classification: classifies severity malnutrition based on weight for age. Waterlow Classification classifies malnutrition based on wasting and stunted growth				
Gomez classification	Weight For Age (%)	Malnutrition			
	91 - 100	Normal			
	76 - 90	1st degree			
	61 - 75	2nd degree			
	< 60	3rd degree			
Waterlow classification	S = Stunted W= Wasted	Malnutrition			
	Height For Age (S)*	Normal	Mild	Moderate	Severe
		95	90 - 95	85 - 90	85
	Weight For Age(W)*	90	80 - 90	70 - 80	70

Indicators		
Wasting	Low Weight for Height	Acute Malnutrition Recent Illness or Food Deficit
Stunting	Low Height for Age	Chronic Malnutrition Prolonged Or Chronic Illness
Underweight	Low Weight for Age	Both Acute and Chronic Illness

PROTEIN ENERGY MALNUTRITION		
Features	Kwashiorkor (Protein Deficit)	Marasmus (Protein and Total Calorie Deficit)
Age and Occurrence	1 – 3 Years, Less Common	6months – 1 Yr., More Common
Face	Edematous / Swollen	Monkey Like
Skin Changes	Flaky Paint Dermatitis	Uncommon
Hair Changes	Flag Sign	Less Marked
Liver	Fatty Liver	Normal Or Atrophic
Edema	Present	None
Mental Status	Normal	Irritable
Infection and Recovery	More Infection, Slow Recovery	Less Infections, Fast Recovery
Appetite	Good	Poor
Wasting and Growth Retardation	Present. Mortality -- high in early stage.	Marked Wasting. Low mortality

Child Physical Abuse

can present with features **resembling Malnutrition i.e., Wasted/Stunted**

But Child may be **Unresponsive, Not following** Command given or **Bruises** on body.

COLLAGEN

- **COLLAGEN is Most Abundant Protein in Body**; types & Collagen diseases are given below.
- **Glycine** is more abundant in Collagen followed by proline and lysine.
- **Most Abundant Protein inside Cell is ACTIN**, whereas inside body abundant in Collagen.
- **Hydroxy proline** is used for **Lab Quantification of Collagen**. **VIT C** is important for it.
- Type 1, 2, 3 & 5 are fibrillary collagen while Type 4 is network forming collagen or non-fibrillary type.
- **Collagen Cross Linking ↑ with Age** while **Elastin** cross linking remains **normal**.
- Dermal Collagen + Elastin dec with Age. Elastin is present in ligaments and lungs.
- **Elastin** is rich in **NON-HYDROXYLATED** glycine, Proline & Lysine while **hydroxylated forms in Collagen**.
- **Fibrillin or elastin is abnormal in Marfan Syndrome and emphysema**.
- **Hypertrophic Scar** has type 1+3 Collagen while **Keloids have type 3 collagen**.
- **Homocystinuria**: low IQ, downward lens dislocation as compared to **Upward in Marfan**

Type 1 Collagen:

90% in human body, present in Skin, **bone**, tendons, ligaments, late wound healing, scar / hypertrophic scar, fibrocartilage, and cornea. **Abnormal Type 1 collagen is seen in osteogenesis imperfecta.**

Type 2:

cartilage: hyaline and elastic, vitreous body of eye

Type 3:

blood vessels, uterus, **reticulin**, Fetal tissues and internal organs of body, early wound healing, keloids, and hypertrophic scar

















Type 4:

Basement membrane. **Abnormal type 4 present in Alport syndrome.**

Type 5:

synovium, tendons, ligament, muscle

COLLAGEN DISORDERS

Marfan syndrome (AD)	 Autosomal dominant FBN1 gene mutation on chromosome 15.  Inherited defect of Fibrillin.  Leads to defective Fibrillin-1 which Forms sheath around elastin and Sequesters TGF-B.  Presents with Tall stature, upward Lens dislocation Hyperextensible joints, Mitral Prolapse, aortic Dissection
Ehler Danlos syndrome (AD/AR)	 Collagen synthesis defect  Presents with Rubbery skin , Hypermobile joints, Large Vessel/ Organ Rupture  Classical: type-V collagen mutation  Vascular type: Type III Collagen Mutation  Hypermobility type is the Most common type
Osteogenesis imperfecta (AD)	 Collagen-triple helix defect, most commonly COL1A1/COL1A2A involved.  Dec production of otherwise Normal type 1 collagen  Presents with Blue sclera , Fractures, Hearing Loss, Dental malformations
Menke's disease (X-Recessive)	 Collagen Cross-linking defect.  Dec activity of Lysyl oxidase due to impaired Cu absorption and transport.  Defective Menke's protein- ATP7-A  Presents with Brittle, kinky Hair, Growth delay, Hypotonia and Cerebral aneurysm

IV FLUIDS & ELECTROLYTE IMBALANCES

Isotonic fluids	Have same composition as that of our internal environment. Cell size remains same e.g., RL & NS Used in BAD: Burns, blood loss, anaphylaxis/sepsis, dehydration.	
	Normal Saline (NS)	<ul style="list-style-type: none">❖ Composition: 0.9% NaCl = 9gm NaCl / 1000ml DW❖ 9 gm /100ml DW (OR) 900mg/100ml DW.❖ All 4 of the compositions given above are same for NS.❖ <u>Indications:</u>❖ IV Hydration (Vomiting), Dehydration in diabetics, Maintenance Fluid, Paradoxical Aciduria – NS or Darrow solution.❖ Shock, Sepsis or Hypotension.❖ Hypovolemic hyponatremia with blood transfusion❖ <u>Contraindications:</u>❖ CHF, ESRD, SIADH, Metabolic acidosis
	Ringer lactate	<ul style="list-style-type: none">❖ <u>Prefer RL over NS in:</u> IV Hydration (Diarrhea), Dehydration, Maintenance Fluid, Shock, Sepsis or Hypotension, Blood loss ($3 \times \text{RL} > 3 \times \text{NS}$)❖ <u>Contraindications:</u>❖ Metabolic alkalosis❖ Severe renal failure, Liver failure❖ Massive blood transfusion, Hyperkalemia❖ Hypercalcemia
Hypotonic fluids	<ul style="list-style-type: none">❖ dilute solutions that cause the cells to swell e.g., 0.45% saline, Dextrose water.❖ Used in pure water deprivation → 5% Dextrose. Never use dextrose sol for diabetics	
Hypertonic fluids	<ul style="list-style-type: none">❖ Concentrated solutions that cause the cells to shrink e.g., 3% hypertonic saline.❖ 3% NS is used in severe hyponatremia, cerebral edema, ketosis and overload of fluid	

Electrolyte	Function	Relationship	Imbalances
Sodium (Na⁺)	Maintains B.P, blood volume and fluid balance	Na and K have inverse relation. ⬆ Na, ⬇ K	<ul style="list-style-type: none"> ○ Normal serum Sodium = 135-145 mEq/L ○ Hypernatremia: inc BP, edema, irritability ○ Hyponatremia: low BP, Seizures, coma ○ Dec height of action potential.
Potassium (K⁺)	Maintains heart and muscle contraction	K is Inverse with Na but directly with Mg, ⬆ K, ⬆ Mg	<ul style="list-style-type: none"> ○ Normal serum K = 3.5-5 mEq/L ○ Hyperkalemia: muscle weakness, Tall T wave on ECG, wide QRS complex ○ Hypokalemia: U wave, flat/inverted T wave, ST depression. ○ U wave – specific feature of hypokalemia.
Magnesium (Mg²⁺)	Keeps muscle cells relaxed after contraction	Direct relationship with K ⁺ , Ca ²⁺ ⬆ Mg, ⬆ K, ⬆ Ca ²⁺	<ul style="list-style-type: none"> ○ Normal serum Mg = 1.5-2.5 mEq/L ○ Hypermagnesemia: bradycardia, low Bp, low RR, Weak pulse, too high Mg → depressed DTRs ○ Hypomagnesaemia: arrhythmias, high Bp, tachycardia, symptoms of low Calcium
Calcium (Ca²⁺)	Bone strength, aids in clotting, helps in muscle contraction	Direct relationship with Mg But Too much Mg can reduce serum Ca levels by decreasing PTH.	<ul style="list-style-type: none"> ○ Normal serum Ca = 8.5-10.5 mEq/L ○ Hypercalcemia: Renal stones, bone pain, psychiatric symptoms, depressed DTRs ○ Hypocalcemia: Trousseau sign +Ve, tetany Chvostek sign +Ve, risk of fracture

ARTERIAL BLOOD GASES (ABGS)

Radial artery sample is used in routine practice and blood is heparinized.

Parameters	Normal	Abnormal	
PH	7.35 – 7.45	< 7.35 – acidosis	>7.45 – alkalosis
Paco2	35 – 45mmhg	< 35mmHg – alkalosis	> 45mmhg – acidosis
Pao2	>90mmhg	75 – 89 mild hypoxia	< 75mmhg -- severe hypoxia
Hco3	22 – 26	< 22mmHg -- acidosis	>26mmHg -- alkalosis
Sao2	94 – 98 %	-	-
Base Excess	-2 to + 2	-	-

INTERPRETATION OF ABGS

- Look at the PH (if low –acidosis and if high PH – alkalosis)
- Identify that which component (PCO₂ / HCO₃) matches PH : look at CO₂ first
- Low PH and high CO₂ = Resp acidosis
- High ph and low co₂ = Resp alkalosis
- Low ph and low bicarbs = met acidosis
- High ph and high bicarbs = met alkalosis
- Find that if the unmatched component i.e pco₂ / hco₃ is within normal range
- Lungs compensate by hypoventilation or hyperventilation
- Kidneys compensate by excreting excess acid and bicarbs or retaining these .
- If unmatched component is Within normal range = uncompensated
- If that is Outside normal range = compensated
- Find that if the unmatched component has compensated enough to return pH back to normal
- Ph in normal range = fully compensated
- Ph not in normal range = partially compensated (ph is never normal in this case)

Four Basic types of acid base disorders are as follows :

1. Metabolic Acidosis – most common abnormality in clinical set up .
2. Metabolic Alkalosis – has a limit for compensation or least compensated (as there is a limit for hypoventilation).
3. Respiratory Acidosis
4. Respiratory Alkalosis

Mnemonics = ROME → Respiratory Opposite & Metabolic Equal/Same

Respiratory OPPOSITE Resp disorders vary with CO ₂	Ph High Co ₂ low HCO ₃ Normal if compensated	Resp Alkalosis
	Ph low Co ₂ high HCO ₃ Normal if compensated	Resp acidosis
Metabolic EQUAL Met disorders vary with Hco ₃	PH High HCO ₃ high Co ₂ normal if compensated	Met alkalosis
	PH low HCO ₃ high Co ₂ normal if compensated	Met acidosis

Disorder	Causes	Clinical features	Management
Metabolic Acidosis	<ul style="list-style-type: none"> ○ DKA ○ Methanol Poisoning ○ Aspirin Toxicity ○ Acute Or Severe Diarrhea, ○ Renal Failure ○ Ethanol/Ethylene Glycol Ingestion 	<ul style="list-style-type: none"> ○ Compensatory hyperventilation or Kussmaul Breathing ○ Nausea / Vomiting ○ Diarrhea – acute/severe ○ Hypotension ○ Headache ○ Peripheral Vasodilation 	<ul style="list-style-type: none"> ○ Treat underlying cause. ○ Dialysis In Renal Failure ○ Insulin, Fluids in DKA ○ Anti Diarrheal Agents ○ Assess Electrolytes – High K+
Metabolic Alkalosis	<ul style="list-style-type: none"> ○ Prolonged Severe or Uncontrolled Vomiting ○ Chronic Diarrhea ○ Bulimia Nervosa ○ Bicarbs Ingestion ○ NH₄Cl Ingestion 	<ul style="list-style-type: none"> ○ Hypoventilation ○ Tremors, Tetany ○ Hypokalemia ○ Restlessness, Confusion ○ Dysrhythmia, Cramps 	<ul style="list-style-type: none"> ○ Anti Emetics ○ Stop Diuretics ○ Monitor Ca And K
Respiratory Acidosis	<ul style="list-style-type: none"> ○ COPD ○ Pneumonia ○ Neuromuscular Diseases like GBS and Myasthenia. ○ CNS Depression (Opioids Overdosage) ○ Thoracic Cage Anomalies E.g. Kyphoscoliosis 	<ul style="list-style-type: none"> ○ Hypoventilation ○ Hyperkalemia ○ Muscle Weakness ○ Tachycardia ○ Drowsiness 	<ul style="list-style-type: none"> ○ 2 – 4 L Oxygen ○ Maintain Airway ○ Prop Up ○ Fluids
Respiratory Alkalosis	<ul style="list-style-type: none"> ○ Hypoxia and High Altitude ○ Status Asthmaticus ○ Pulmonary Embolism ○ Mechanical Ventilation ○ Hyperventilation Syndrome ○ Salicylates Overdose, Anxiety ○ Head Trauma, Sepsis and Fever 	<ul style="list-style-type: none"> ○ Hyperventilation ○ Hypokalemia ○ Numbness And Tingling ○ Lethargy And Confusion ○ Tachycardia, Tachypnea ○ Light Headedness 	<ul style="list-style-type: none"> ○ Paper Bag Rebreather ○ Monitor for Over Ventilation ○ Watch K And Ca Levels

ANION GAP (AG)

- Anion gap represents Unmeasured anions in the serum.
- Anion gap is the difference between measured cations and measured anions.
- Anion gap is the difference between unmeasured anions and unmeasured cations.
- Normal anion gap is 8 -12 mEq/L .

$$\text{Formula of AG} = \text{Na} - (\text{Cl} + \text{HCO}_3)$$

Met acidosis may be of normal AG or high AG.

High anion gap met acidosis is seen in:

- DKA, uremia, methanol, salicylates, lactic acidosis, ethylene glycol , paraldehyde , isoniazid

Normal anion gap met acidosis is seen in:

- Diarrhea, CKD, intestinal or biliary fistula, renal tubular acidosis, ureterosigmoidostomy


EMBRYOLOGY

IMP TOPICS:

Gem Layer Derivatives, Pharyngeal Apparatus, Fertilization, Placenta, Tongue, Renal system, Post Natal Derivatives

Embryonic Period	<ul style="list-style-type: none"> The first 8 Weeks are embryonic period. Most sensitive phase of development. Organ's development occurs from 3 basic Germ layers. Organs are formed by the end of the 8th week or 2 months. Major Organ defects & Teratogenesis occur during the embryonic period.
Fetal Period	<ul style="list-style-type: none"> Period After 8 Weeks of development which includes further growth and development.

PRE- FERTILIZATION & FERTILIZATION EVENTS

- Gametogenesis is development of male and female haploid gametes/Germ cells i.e., Sperms & eggs.
- They are derived formed from **primordial germ cells in epiblast** during 2nd weeks and move to the wall of yolk sac. PGCs formed at end of 2nd/beginning of 3rd week.
- PGCs migrate from the wall of yolk to arrive at gonads at end of 5th/ beginning of 6th week.
- For Exam: Prefer 3rd Week for formation & 6th Week for migration.
- Regarding primordial germ cells (46,2N) (Follow this Sequence):
 Derived from → Epiblast > Ectoderm > Endoderm of Yolk Sac

SPERMATOGENESIS		OOGENESIS	
<ul style="list-style-type: none">Sequence of events that transform Spermatogonia into Sperm/spermatozoa.Spermiogenesis:Process of Formation of sperms from spermatidsSteps Of Spermatogenesis:<ul style="list-style-type: none">Primordial Germ cells (46,2N) from wall of yolk sac arrive in Testes at 6th week and stay dormant till Puberty.PGCs differentiate into Type A Spermatogonia at puberty.Type A form additional Type A & type B Spermatogonia by Mitosis.Type B undergo Mitosis into primary Spermatocytes.Primary Spermatocytes undergo 1st meiotic division to form 2 haploid 2ndry spermatocytes.Secondary Spermatocytes undergo 2nd meiotic division to form 4 haploid spermatids.Spermatids undergo Spermiogenesis to form 4 mature sperms.		<ul style="list-style-type: none">Sequence of events converting primitive germ cells i.e., oogonia into mature Ovum/ Egg.PGCs from wall of yolk sac arrive at ovary in 6th week of development to differentiate into Oogonia (2N)Oogonia enters meiosis I to form primary oocyte.Primary oocyte Dormant in prophase(diplotene) of meiosis 1 until puberty.During Ovarian Cycle:<ul style="list-style-type: none">Primary Oocyte completes Meiosis 1 To form secondary oocyte.Secondary Oocyte remains arrested in Metaphase of meiosis 2 Until Fertilization.At Fertilization:<ul style="list-style-type: none">secondary Oocyte completes Meiosis - II to form a mature oocyte & second Polar Body.	
SPERM	<ul style="list-style-type: none">1 Primary spermatocyte forms 4 spermatozoaSpermiogenesis is formation of spermatozoa from spermatids.Fertile man produces 3.5 ml semen and 350 millionsperm per ejaculate, 1 mL = 100 million sperms.Two testes produce 120 million sperms per day.Infertile male has sperm count less than 20million/ml.Formation of primary spermatocyte begin at puberty.Head part of spermatozoon is formed by nucleus.Acrosomal cap of spermatozoon is formed by Golgi body.Axial filament and tail of sperm is formed by centrosome and centriole.Spermatogenesis is completed in 64 days. Length of fully mature sperm is 50 microns.Sperms have capacity to fertilize ovum until 48 hours.		
OVUM	<ul style="list-style-type: none">Primary oocyte forms 1 ovum. In ovum at ovulation 2nd meiotic division is in progressAt ovulation ovum is at Metaphase of meiosis II		

	<ul style="list-style-type: none"> ○ Primary oocyte remains dormant for 12 to 40 years. ○ At the time of ovulation ovum is Secondary oocyte ○ At 5 month of intrauterine life there are 7 million eggs. ○ At puberty there are 40,000 primary oocytes. Oocyte present in ovary at birth are 4 lacs. ○ A Female ovulates 480 eggs during reproductive life ○ All primary oocyte is formed at 5th month of intrauterine life. ○ Secondary oocyte completes its secondary meiotic division at time of fertilization after ovulation. ○ First meiotic division is completed before ovulation. ○ Germinal epithelium of ovary is simple cuboidal. ○ Zona pellucida is seen in primary follicle. Ovulation takes place from griffin follicle. ○ Secondary oocyte is 150 microns. ○ Ovum remains viable up to 12 to 24 hrs. ○ Corpus leuteum of menstruation remain active till 2 weeks. ○ Corpus leuteum of pregnancy active till 3 months.
--	---

FERTILIZATION

Formation of zygote from fusion of sperm and egg at ampulla of fallopian tubes

Three phases:

1. **Sperm penetration of corona Radiata** → includes Capacitation & acrosomal reaction.
Capacitation: helps in Movement of sperm by washing head through removal of glycoprotein coat.
Acrosomal Reaction: Acrosome of sperm perforates Corona Radiata.
2. **Sperm Binding and Penetration of Zona Pellucida:** sperms contacts with membrane of 2ndry oocyte.
3. **Fusion of Sperm & Oocyte:** 2ndry oocyte completes 2nd meiotic division as soon as the sperm contacts it and forms mature ovum. Male & Female Pro nuclei form which fuse to form Zygote.

Remember that:

- ✚ **Fertilization occurs in Ampulla of uterine tubes.**
- ✚ **Most common site of ectopic pregnancy is also fallopian /uterine tube.**
- ✚ **The least common site for ectopic pregnancy is cervix.**

WEEKS OF DEVELOPMENT

(For exam point of View, 1st to 4th week is important).

1st Week	<ul style="list-style-type: none"> ❖ Blastocyst Implantation (6th day) at posterior superior wall of Uterine cavity in the functional layer of endometrium during Secretory phase of Menstrual Cycle ❖ Fertilization → Zygote → Cleavage → Blastula → Morula (16 blastomeres) → Blastocyst → implantation ❖ Zone pellucida must degenerate for blastocyst implantation. ❖ Blastocyst gives embryoblast (from inner cell Mass) which forms embryo and trophoblasts from Outer cell mass which form part of placenta. ❖ Trophoblasts differentiate into inner cytotrophoblasts & outer Syncytiotrophoblast (source of HCG) ❖ Cytotrophoblasts are mitotically active and Uninucleated. ❖ Syncytiotrophoblast - not mitotically active. ❖ Blastocele becomes the Yolk sac. ❖ Blastomeres cells are Totipotent up to 8 celled Stage i.e., they can form complete embryo at this stage. ❖ Embryoblast cells are multipotent → form 3 germ layers i.e., Ectoderm, endoderm, and mesoderm
2nd Week	<ul style="list-style-type: none"> ❖ Inner cell mass of Blastocysts forms epiblast and hypoblast which lead to bilaminar germ disc formation and this bilaminar disc forms Embryo proper. ❖ Epiblast (Dorsal): <ul style="list-style-type: none"> ✚ High Columnar cells which contribute to the Amniotic cavity formation and Primordial germ cells. ✚ Extraembryonic mesoderm is Derived from epiblast. ❖ Hypoblast(Ventral): <ul style="list-style-type: none"> ✚ Small Cuboidal cells which form Primary YOLK Sac/ Exocoelomic cavity/Hausermembrane and Endoderm. Extraembryonic Coelom is derived from Hypoblast

3rd week	<ul style="list-style-type: none"> ❖ Trilaminar Germ Disc Formation → Ectoderm + Mesoderm + Endoderm Formation. ❖ Heart Development Starts but Doesn't Beat. ❖ Primitive Streak & Notochord Formation. ❖ Notochord Appear at Age Of 16-18 Day → Primary Organizer/Inducer During Organogenesis. ❖ Notochord Extends from Pre-Chordal Plate to Primitive Node. ❖ Notochord Adult Derivative is Nucleus Pulposus. ❖ Primitive Streak Appears At 21st Day/3wks Is the Site of Involution of Epiblast Cells to Form Mesoderm ❖ Cells From Primitive Streak Don't Become Amnioblasts. ❖ Sacroccygeal Teratoma Arises from Remnants of Primitive Streak. ❖ In 3rd Weeks Neural Plate Is Induced by Notochordal Process & Associated Mesoderm
4th Week	<ul style="list-style-type: none"> ❖ Pharyngeal Arches become visible + Heart begins to Beat + 4 limb buds formation. ❖ At the beginning of the 4th week, the somite's (4) are well formed, and the neural tube is also formed. ❖ but it is opened at the rostral and caudal neuropores. Closure of Neural tube at 23rd day ❖ Closure of cranial neuropores occur at 25th day but Caudal neuropores close at 27th day. ❖ Upper limb buds become recognizable during week 4 and the lower limb buds become present by the end of week 4 (day 28). The patterning of the limb development is regulated by Homeobox genes. ❖ The upper limb buds form opposite the caudal cervical segments and lower limb buds form opposite the lumbar and upper sacral segments. ❖ Stomach And Foregut Organ formed. ❖ Pronephros develop earlier, while mesonephros develop late. ❖ Respiratory diverticulum formed. Laryngotracheal Groove forms at 4th week <u>EYE</u> ❖ Otic groove forms at 22nd day in Diencephalon. ❖ Optic vesicle develops at about 28th day. Surface ectoderm forms Lens placode by 27th to 29th day ❖ By 30th day lens Vesicle is formed
5th week	<ul style="list-style-type: none"> ❖ Metanephros Begin to Work and Gonads Pronephros Regress. ❖ Tracheoesophageal Fold Formed and Bronchial Buds Enlarge. ❖ Bones Appear During Week 5 As Mesenchymal Condensations in The Limb Buds. ❖ Upper Limbs Show Regional Differentiation with Developing Hand Plates.
6th week	<ul style="list-style-type: none"> ❖ Midgut Herniate Through Umbilical Cord. ❖ Primordial Germ Cells Migrate into Gonads ❖ Trachea And Esophagus Separate From Each Other ❖ Mesenchymal Models of The Bones in The Limbs Undergo Chondrification to Form Hyaline Cartilage. ❖ The Clavicle Develops by Intramembranous Ossification and Later Develops Articular Cartilages.
7th week	<ul style="list-style-type: none"> ❖ Limb Rotations Begins
8th week	<ul style="list-style-type: none"> ❖ Week 8 (Last week of embryonic life) ❖ At the beginning of week 8, The digits of the hand are short and webbed. Notches develop between the digital rays of the feet. ❖ At the end of week 8, there are distinct regions in the limbs, with long fingers and distinct toes.
9 – 12th weeks	<ul style="list-style-type: none"> ❖ The fetus has short legs and small thighs at the beginning of week 9. ❖ By the end of week 12, the upper limbs have reached their final relative length but not the lower limbs. ❖ Primary ossification centers are present in all long bones ❖ Order of ossification: 1st Clavicle and 2nd femur.
34 – 38th weeks	<ul style="list-style-type: none"> ❖ Secondary ossification centers appear in the epiphyses. ❖ The first ones to appear are in the distal femur and the proximal end of the tibia, at the knee joint. ❖ The epiphyseal cartilage plate intervenes between the diaphysis and epiphysis. When it is replaced around age 25, growth of the bones ends.
Remember	<ul style="list-style-type: none"> ▪ 1st -6th week -- embryo remains undifferentiated. ▪ 7th week -- begins to differentiate. ▪ 10th week -- Male and female external genitalia recognized (sex determination). ▪ 20th week -- Phenotypic differentiation complete.

GERM LAYERS DERIVATIVES	
ECTODERM	<ul style="list-style-type: none"> Makes you eye catching & attractive → Skin, Hair, nails, lens, Cornea, teeth enamel. Glands: Sweat, Sebaceous, mammary, parotid & lacrimal. CNS & PNS from neural crest & neural tube of ectoderm. Derivatives of Neural Crest Cells: <ul style="list-style-type: none"> PNS, Autonomic ganglia, Schwann cells, Adrenal Medulla, Melanocytes, Facial + laryngeal Cartilage, Odontoblasts, Pia & arachnoid matter From neural tube of ectoderm: <ul style="list-style-type: none"> Brain & spinal Cord, Motor neurons, Retina, Pituitary gland (Also from Diencephalon) IMP BCQs <ul style="list-style-type: none"> Adrenal Medulla is derived from Neural crest cells while adrenal Cortex from Mesoderm. Dura matter is Mesodermal in Origin whereas Arachnoid + Pia is derived from Neural Crest. Parotid gland is of ectodermal Origin but submandibular & salivary from Endodermal Origin.
ENDODERM	<ul style="list-style-type: none"> Linings of tubes, mainly the structures You can't touch without your hands. Lining of Oral cavity from mouth to anus, nose, urethra & vagina. Pharynx, Stomach, intestines, thyroid, Trachea epithelial parts, Lungs, Liver, pancreas, and, bladder.
MESODERM Mnemonics (GONADS)	<ul style="list-style-type: none"> Genitourinary + Renal system Others -- Bones, muscle, connective Tissues, Serous Lining of body cavities, CVS system. Notochord → nucleus Pulposus Adrenal cortex, Dura matter, Spleen Mesoderm gives rise to Paraxial, intermediate, and lateral plate mesoderm. <ol style="list-style-type: none"> Paraxial Mesoderm: forms Somites Intermediate Mesoderm gives rise to Urogenital system (BCQ) Lateral Plate mesoderm splits into Somatic + Splanchnic layer by formation of intra-embryonic coelom. <ul style="list-style-type: none"> Somatic Layer + Ectoderm Form Body Wall/ Somatopleura e.g Parietal Covering of Pleura & Pericardium. Splanchnic Layer + Endoderm Form Gut Tube/ Splanchnopleura e.g Visceral Layer of Pleura/Pericardium. Heart & Major vessels are derivative of Splanchnic layer of Lateral plate Mesoderm.

SOMITES

- Develop from paraxial mesoderm and first appear at 20th day in cervical region.
- At 20th days 1 to 4 somite's are formed. The caudal most pairs Disappear giving net count of 37-38 Pairs of somites while total formed are 42-43 Pairs initially.
- Give rise to dermis, muscles + vertebral column/ axial skeleton.
- Paraxial mesoderm forms a segmental series of tissue blocks on each side of Neural tube known as Somitomeres in the head region. From the Occipital region caudally Somitomeres → Somite
- Somites subdivide into: Sclerotome, Dermatome, and myotomes.**
 - Sclerotome** is the ventromedial part that forms Mesenchyme or embryonal connective tissue, that give rise to vertebrae of the vertebral column, rib cage and part of Occipital bone.
 - Dermomyotome:** The dorsolateral part that forms Skeletal muscle, cartilage, tendon, and Skin of the back.
- The 1st pair of somites arise in the occipital region of embryo at approximately 20th day of development.
- From here new somites form at a rate of approximately 3pairs/ day Until at the end of fifth week -- 42 to 44 pairs. These are:
 - Occipital = 4 pairs -- give rise to tongue (BCQ)**
 - Cervical = 8 pairs -- give rise to diaphragm (BCQ)**
 - Thoracic = 12 pairs, Lumbar = 5 pairs, Sacral = 5 pairs and Coccygeal = 8- 10 pairs
 - The first Occipital and the last 5- 7 Coccygeal somites disappear.
 - During the period of development, the age of embryo is expressed in no. Of somites

PREGNANCY, PLACENTA, UMBILICAL CORD & AMNIOTIC FLUID

Gestational Age	○ Period from 1 st day of LMP Calculated by adding days into LMP.
Fetal Age	○ Period from day of conception . So Fetal age is Less than gestational age by 2 weeks as conception occurs later.
EDD	○ Calculated from LMP by adding 9months + 7 days
Ectopic Pregnancy	○ Most common site is Fallopian tube but least common is Cervix. ○ When ruptured presents with Pain abdomen, Tachycardia, Hypotension, Pain in hypochondrium/ iliac fossa.

Human Chorionic Gonadotropin (HCG)	<ul style="list-style-type: none"> ○ Secreted from syncytiotrophoblasts detected on maternal Blood at 08th day while in urine at 10th day. ○ Stimulates progesterone production by corpus luteum ○ ↓ HCG in Spontaneous abortion & ectopic pregnancy ○ ↑ HCG in Multiple Pregnancy, Hydatiform Mole, Choriocarcinoma ○ In ectopic Pregnancy HCG is raised but that raised levels are less than Normal for Normal Pregnancy
Human Placental Lactogen (HPL)	<ul style="list-style-type: none"> ○ Also called Growth Hormone of fetus. Induces lipolysis. ○ GH levels remain normal in pregnancy.
Alpha Feto Protein (AFP)	<ul style="list-style-type: none"> ○ Fetal albumin produced by hepatocytes. Assayed at 14-18th wk. ○ ↓ AFP seen in Down's syndrome ○ ↑ AFP seen in Anencephaly, NTDs (Spina Bifida)





PLACENTA

- Site of **Nutrient & gas** exchange b/w mother and fetus
- **Placenta secretes HCG, HPL, estrogen, estradiol, progesterone, inhibin.**
- Substances Crossing Placenta → TORCH infections i.e., Toxoplasma, others (Syphilis), Rubella, CMV, Herpesviruses, IgG, propylthiouracil, methimazole.
- Can not Cross Placenta → Insulin, heparin, thyroxine, methyldopa & some bacteria's etc.
- Placenta is Formed by following components.
- I. **Maternal Component of placenta formed from → Decidua Basalis** (Derived from endometrium)
- II. **Fetal Component from → Cytotrophoblasts & Syncytiotrophoblast.**

Decidua:

- Specialized maternal tissue which forms Placental Bed .it differentiates into following 3 layers:
- Decidua Basalis: It is under site of Implantation which forms placenta.
- Decidua Capsularis: covering ovum.
- Decidua Parietalis: Lining of rest of uterine cavity

Types of Placenta:

-  **Placenta Previa:** placenta attaches **Lower uterus covering Internal Os**
-  **Placenta Accreta:** when placenta gets **implanted into myometrium** but doesn't penetrate it.
-  **Placenta increta:** placenta implanted **deep** into myometrium i.e., penetrated it.
-  **Placenta Percreta:** when it is implanted **through wall of uterus** i.e., **Penetrates Serosa** as well.

Gold standard for placenta previa → Transvaginal ultrasound (TVS)

Chorionic Villi

1. **Primary Villi:** made of Cytotrophoblasts + Syncytiotrophoblasts.
2. **Secondary Villi:** when Mesenchymal Core attaches to cytotrophoblasts & syncytiotrophoblasts
3. **Tertiary villi:** when **Blood vessels are formed in it.**

Amniotic Fluid	<ul style="list-style-type: none"> ❖ Composed of water, electrolytes, fat, protein, amino acids, fetal urine, faeces & lung fluid. Normally 500ml circulates through amniotic sac per hour. ❖ At 34th weeks → 800ml while at Term is it 600-800ml. Prefer 800 mL. Oligohydramnios: AF < 400 ml due to inability of Kidneys to excrete urine. Fundal height is less than normal. ❖ Causes are Renal Agenesis, Uteroplacental insufficiency, Rupture of Membranes. Polyhydramnios: AF > 2000 mL due to inability of fetal swallowing ❖ Causes: Anencephaly, Spina bifida, Esophageal/duodenal atresia, Maternal infection, DM ❖ Structures Passing through Umbilical Ring → yolk sac, connecting stalk + allantois.
Urachus Vs Allantois	<ul style="list-style-type: none"> ❖ Adult derivative of allantois is median umbilical ligament. ❖ Most common remnant of allantois is urachal cyst; also patent local area is urachal cyst. ❖ patent lumen of allantois = urachal fistula. ❖ patent lumen in superior/inferior part = urachal sinus. ❖ urine of a pt. is dribbling from umbilicus cause is patent urachus.
Umbilical Cord	<ul style="list-style-type: none"> ❖ 50-60cm Long pearly white, containing Connective Tissue i.e., Wharton jelly connecting fetus & placenta ❖ Cord Has 2 arteries + 1 veins. VASA VASORUM is Absent in these vessels. ❖ Umbilical Arteries carry Deoxygenated Blood. Umbilical Vein carries oxygenated. ❖ Umbilical vein has 80% O₂ saturation + 30mmg O₂ pressure. It carries blood from Fetus to Placenta ❖ Right umbilical vein disappears while left umbilical vein forms ligamentum teres.

HEAD & NECK

Pharyngeal Apparatus

- ❖ **Consist of Arches, pouches, grooves & Membranes. Observed in fourth weeks of development.**
- ❖ Pharyngeal **Arch 5 & Pouch 5** completely **regress** in humans.
- ❖ Remember it like, **CAP** from Outer to inner.
- ❖ Clefts derived from **Ectoderm**.
- ❖ Arches derived from **Mesoderm & Neural Crest cells**.
- ❖ Pouches derived from **Endoderm**.

Pharyngeal Cleft and Membrane Derivatives:

- ❖ **1st cleft** gives rise to **External auditory meatus**.
- ❖ **2nd - 4th** → Obliterated. Or form **Cervical Sinus** anterolateral to Sternocleidomastoid muscle.
- ❖ **1st membrane** forms **Tympanic** membrane. The rest 2- 4th are **Obliterated**.

Pharyngeal Pouches Derivatives

1st POUCH	Tympanic cavity, Eustachian tube/auditory tube and Mastoid
2nd POUCH	Epithelial Lining of palatine tonsils (T for Two & Tonsils)
3rd POUCH	Ventral wing → Thymus Dorsal Wing → inferior Parathyroid glands
4th POUCH	Ventral → Ultimobranial body → give Para follicular/C Cells of thyroid. Dorsal → Superior Parathyroid glands

PHARYNGEAL ARCHES DERIVATIVES (V. IMPORTANT)

Pharyngeal Arch	Artery & Nerve	Muscles	Bone, Cartilage & Ligaments
<u>FIRST ARCH</u> (Mandibular Arch) All with M's and T's	Maxillary artery (Transient) Maxillary nerve V2 Mandibular nerve V3 (Branches of CN V) Chorda tympani	Chew Muscles of Mastication Mylohyoid Anterior belly of digastric Tensor tympani Tensor Veli palatini	Maxillary process: Maxilla, Zygomatic, palatine, Squamous temporal bone Mandibular process: Malleus, incus, stapes Meckel's cartilage Sphenomandibular ligament
<u>SECOND ARCH</u> Stapedial Arch) All with S	Hyoid and Stapedial artery (Transient) Facial nerve	Smile Muscles of facial expression Posterior belly of digastric Stylohyoid and Stapedius	Lesser horn and Upper part of body of hyoid bone Stapes Richter's cartilage Stylohyoid ligament
<u>THIRD ARCH</u>	Proximal Internal carotid artery Common carotid artery Glossopharyngeal nerve	Swallow stylishly Stylopharyngeus	Greater horn or cornua of hyoid bone and Lower part of body of hyoid bone
<u>FOURTH ARCH</u>	On right: Rt subclavian On Left: Arch of aorta Superior laryngeal nerve (Branch of Vagus nerve)	Muscles of soft palate (except tensor veli palatini) Cricothyroid Cricopharyngeus	Thyroid cartilage Epiglottis cartilage
<u>SIXTH ARCH</u>	On right: Right Pulmonary On left: ductus arteriosus and left pulmonary artery. Recurrent laryngeal nerve (Branch of vagus nerve)	All intrinsic muscles of larynx Except Cricothyroid Skeletal muscles of esophagus	Cricoid cartilage Arytenoid cartilage Cuneiform cartilage Corniculate cartilage

Hints to Remember pharyngeal arches derivatives.

- Cranial Nerves of these arches are CN **5,7,9,10**
- Arteries are Branches of **arch of aorta i.e.,** Common Carotid, Subclavian etc.
- **1st Arch** is for **Chewing/mastication**. All **Ms& Ts**
- **2nd arch** is **S** arch i.e., all structures with mostly **S/ smile** → **muscles of Facial expression**
- **3rd arch** for **Stylish swallowing i.e., Stylopharyngeus**
- **4th -6th arches** for **Swallow + Speak**. All **Larynx cartilages + muscles + pharynx** muscles
- **Nerve** of 4th -6th arch is **VAGUS** nerve while for 3rd arch it is Glossopharyngeal Nerve
- **NO** Derivatives from 5th arch – degenerated.

EAR

- External + inner ear arise from ectoderm. Middle ear derived from endoderm
- PINNA+ auricle from 1st+ 2nd arch. Cartilage of ear is elastic; alone Pinna is derived from ectoderm of 1st cleft
- Ear bones/Ossicles from 1st& 2nd arch. Auditory tube, tympanic cavity, mastoid air cells from 1st pouch
- Tympanic membrane basically from All 3 Layers but if in exams if there are options of ectoderm & endoderm together; then prefer it.
- Ossicles develop from Meckel's & Richter cartilage → Mesoderm.
- First part of Ear to reach adult size is inner ear. Inner ear is of same size in Neonates& adults

TONGUE DEVELOPMENT

Oral part	<ul style="list-style-type: none">• Anterior 2/3 develop from 1st pharyngeal arch so general sensation from CN V (Lingual nerve) and Taste/special sensation (SVA) via CN VII (Chorda Tympani)
Pharyngeal part	<ul style="list-style-type: none">• Posterior 1/3 from 3rd & 4th pharyngeal arches.• General and taste sensation of posterior part is via CN IX• Posterior most part is Supplied by VAGUS Nerve
Muscles	<ul style="list-style-type: none">• intrinsic and extrinsic MUSCLES of tongue from myoblast migrated from occipital Somites. Tongue muscles are NOT derived from any pharyngeal arch.• All muscles supplied by Hypoglossal nerve except palatoglossal muscle which is supplied via vagus nerve.

THYROID GLAND

- First gland to be formed in embryo at about 4wks of development.
- Thyroid primordium appears as a median endodermal proliferation in the floor of the pharynx between tuberculum impar and hypobranchial eminence (Indicated by foramen caecum in adult tongue).
- This proliferation is invaginated to form a bilobed diverticulum which descends Ventral to the developing hyoid bone then ventral to the developing larynx. It remains connected to the dorsum of tongue by the thyroglossal duct. Thyroid gland finally reaches its position by seventh week.

Note:

- The thyroid follicles derived from endodermal cells of the thyroglossal Duct.
- The parafollicular (C) cells derived from the ultimobranchial body.
- The true capsule and connective tissue septa derived from mesoderm.

Fate of the Thyroglossal duct:

- The part of duct between hyoid bone and isthmus of the gland gives rise to Pyramidal lobe and levator glandulae thyroideae or may degenerates completely.
- Above the hyoid bone the duct degenerates completely.

Congenital Anomalies of The Thyroid Gland










- 📖 **Thyroid agenesis:** congenital absence of thyroid gland.
- 📖 **Lingual thyroid:** the thyroid fails to descend and lies in the substance of Tongue.
- 📖 **Aberrant thyroid (retrosternal thyroid):** the thyroid descends to reach Thorax.
- 📖 **Thyroglossal cyst:** due to persistence patency of a part of the thyroglossal Duct.
- 📖 **Thyroglossal fistula:** It is acquired due to rupture of infected cyst. Leading to communication between the thyroglossal duct and skin of neck.
- 📖 **Thyroglossal cyst & fistula move with deglutition & protrusion of Tongue.**

CARDIOVASCULAR SYSTEM

- **Heart is 1st organ in developing fetus to become Functional. Starts beating by 4th week.**
- **Heart is derivative of Splanchnic Lateral plate Mesoderm.**
- **Intraembryonic mesoderm is derived from Lateral plate mesoderm.**
- **Endocardial cushions are derived from neural crest cell** separated Atria & ventricles.
- Sinus venosus forms Coronary sinus + Smooth part of RA + Oblique vein of left atrium – Marshal vein.
- RCA arises from Right anterior coronary sinus whereas LCA from Left posterior coronary sinus.

Embryonic Structure	Gives Rise To / Derivative
Primitive atrium	Trabeculated part of right and left atrium
Primitive Ventricle	Trabeculated part of right and left ventricle
Right horn of sinus venosus	Smooth part of right atrium
Left horn of sinus venosus	Coronary sinus
Bulbus cordis	Smooth parts of right and left ventricles
Truncus arteriosus	Ascending aorta and pulmonary trunk
Endocardial cushions	Atrial septum, membranous interventricular septum Av and semilunar valves
Primitive pulmonary vein	Smooth part of left atrium
Right common cardinal + Rt anterior cardinal vein	Superior Vena cava
Posterior, sub cardinal and supra-cardinal veins	Inferior Vena cava

FETAL POST NATAL DERIVATIVES	
Fetal Structure	Derivative
Foramen Ovale	Fossa Ovalis
Ductus arteriosus	Ligamentum arteriosum – near left recurrent laryngeal nerve
Ductus Venosus	Ligamentum venosum
Allantois → Urachus Urachus is part of allantois duct b/w bladder and umbilicus	Median umbilical ligament
Notochord	Nucleus pulposus
Umbilical artery	Medial umbilical ligament
Umbilical vein	Ligamentum teres hepatis – round ligament

AORTIC ARCHES		
<ul style="list-style-type: none">1st Arch: Maxillary artery2nd Arch: Stapedial Artery3rd Arch: C is third letter so remember it like; Common Carotid & internal Carotid.4th arch: on Right: Rt subclavian; on Left: ARCH OF AORTA6TH Arch: ductus arteriosus + Proximal parts of R, L Pulmonary Arteries (BCQ)		
Oxygenated Blood	<ul style="list-style-type: none">It Enters IVC by Ductus Venuses bypassing Hepatic Circulation. Most of highly oxygenated blood reaching heart via IVC is directed via Foramen Ovale into LA	
Deoxygenated Blood	<ul style="list-style-type: none">From SVC it passes through RA to RV. From RV to Main Pulmonary Artery to ductus arteriosus to descending aorta. Shunt due to high fetal pulmonary Resistance.	
Changes in Fetal Circulation after Birth		
Shunt	Functional Closure	Anatomical Closure
Ductus Venosus	Within Minutes after birth	3-7 days after Birth
Foramen Ovale	Within mins after birth	1 year after Birth
Ductus Arteriosus	10-96hrs after birth	2-3 weeks after birth
Which of following Soon closes after Birth ✍ Choose Ductus Venosus		
<div>Key Facts</div> <div><div></div><div><div>↑</div><div>LA pressure than RA pressure causes closure of foramen Ovale.</div></div></div> <div><div></div><div>PGE1&PGE2 keep PDA open, but INDOMETHICIN helps Closure of PDA</div></div> <div><div></div><div>Most common cause of patent foramen Ovale is <div><div>→</div></div> Failure of septum Premium & septum secundum to fuse.</div></div> <div><div></div><div>If above these are not mentioned in exams together; prefer patent septum Secundum.</div></div> <div><div></div><div>Aorticopulmonary septum fuses with muscular ventricular septum to form membranous interventricular septum closing the interventricular foramen.</div></div> <div><div></div><div>VSD is the most common congenital cardiac anomaly usually in membranous septum.</div></div> <div><div></div><div>Defect in left-right dynein leads to dextrocardia; also seen in Kartagener syndrome.</div></div> <div><div></div><div>Right RLN loops around Right subclavian artery.</div></div> <div><div></div><div>left RLN loops around ductus arteriosus/ligamentum arteriosus > arch of aorta</div></div>		

RESPIRATORY SYSTEM

- Develops in **5 states** from **lung bud arising** from Distal respiratory diverticulum in **4th week**.
- Inc vascularity** seen in **Canalicular stage**.
- Bronchogenic cyst** forms due to abnormal foregut budding & dilatation of terminal/large bronchi.
- Type 1 pneumocytes make part of Blood Air Barrier while type2 secrete Surfactant.
- Respiration is capable at 25th week.
- Stages of Fetal Lung development are as follows:**
 - Embryonic Stage: 4 – 7 weeks of development. Trachea + bronchi develop (up to 10)**
 - Pseudo glandular Stage: 5 – 17 wks.** Further Bronchi and bronchioles develop.
 - Canalicular stage: 16 – 26 weeks.** Respiratory bronchioles develop.
 - Saccular stage** from 24 weeks – term alveolar ducts & sacs develop.
 - Alveolar Stage: 36wks – 21 years.** Alveolarization – development of alveoli occurs.

Screening For Fetal Lung Maturity

- By **Lecithin/sphingomyelin ratio (L / S ratio)**
- 2 L/S ratio is healthy but < 1.5 L/S ratio is predictive of neonatal RDS
- RDS is caused by Surfactant deficiency and Inc Surface Tension; can lead to bronchopulmonary dysplasia.
- RDS in premature infants can be prevented by injection **Betamethasone** given to mother.

POTTER sequence	<ul style="list-style-type: none"> ○ Pulmonary hypoplasia (cause of death)
Mnemonics (POTTER)	<ul style="list-style-type: none"> ○ Oligohydramnios ○ Twisted face Twisted skin, Extremity defects, Renal failure (in uterine) ○ Pulmonary hypoplasia is poorly developed bronchial tree with abnormal histology associated with potter sequence/ Lt sides Congenital Diaphragmatic Hernia
Congenital Diaphragmatic Hernia	<ul style="list-style-type: none"> ○ Mostly Lt sided due to Incomplete fusion of Pleuro-peritoneal membranes. (Imp BCQ) ○ Presents with Dyspnea, Tachypnea and sometimes Abdominal viscera pushed into Thorax.

GASTROINTESTINAL SYSTEM

	FOREGUT	MIDGUT	HINDGUT
Derivatives	<ul style="list-style-type: none"> ○ Esophagus ○ Stomach ○ Duodenum - till Ligament of Treitz ○ Liver ○ Gallbladder, Biliary Apparatus ○ Pancreas 	<ul style="list-style-type: none"> ○ Duodenum (2nd – 4th Part) ○ Jejunum, Ileum ○ Caecum, Appendix ○ Ascending Colon ○ Transverse Colon 2/3rd 	<ul style="list-style-type: none"> ○ Distal 1/3rd Transverse Colon, Splenic Flexure ○ Descending and Sigmoid Colon ○ Rectum, and Anal Canal above Pectinate Line
Artery	○ Celiac Artery	○ Superior Mesenteric	○ Inferior Mesenteric Artery
Parasympathetic Innervation	○ Vagus Nerve	○ Vagus Nerve	○ Pelvic Splanchnic Nerves
Sympathetic Innervation	<ul style="list-style-type: none"> ○ Preganglionic: Thoracic Splanchnic Nerves (T5 – T9) ○ Post Ganglionic Cell Bodies: Celiac Ganglion 	<ul style="list-style-type: none"> ○ Preganglionic: Thoracic Splanchnic Nerves (T9 -T12) ○ Post Ganglionic: superior mesenteric ganglion 	<ul style="list-style-type: none"> ○ Preganglionic: Lumbar Splanchnic Nerves L1-L2 ○ Post Ganglionic inferior mesenteric ganglion
Referred Pain	○ Epigastrium	○ Umbilical	○ Hypogastrium

- **Mid Gut Herniation** is physiological, starts at 6th week and completes by 10th wk. Total rotation is 270° Counter/anti-clockwise Around axis of SMA.
- Liver is derived from Ventral foregut bud.
- Hepatocytes derived from endoderm while Kupffer cells from mesoderm.
- Spleen Arises in mesentery of stomach (BCQ) hence is mesodermal.
- **Esophageal Atresia**
Atresia with distal Tracheoesophageal fistula is the most common tracheoesophageal anomaly. Often associated with polyhydramnios. (BCQ)
Neonates **drool** > choke > vomit with 1st feed. Failure to Pass NG tube.
- **Duodenal Atresia**
Shows Double bubble sign on X ray -- associated with DOWN syndrome.
- **Jejunal/ileal Atresia.**
Triple bubble Sign (dilated stomach, duodenum, proximal jejunum)
- **Hypertrophic Pyloric Stenosis**
thickening of circular muscles at Pyloric sphincter.
Presents with non-bilious projectile vomiting at 2–6-week-old infant.

- Palpable Olive shaped Mass in epigastrium with visible peristaltic waves.
- Most common cause of Gastric Outlet obstruction in infants.
- Results in Hypokalemia hypochloremic Metabolic alkalosis (BCQ)
- USG shows thickened pylorus and Target sign; Treated by pyloromyotomy.

➤ **PANCREAS**

- Dorsal bud: forms Head, Body, Tail, isthmus, Accessory duct
- Ventral bud: Main part of head, uncinate process, main pancreatic duct
- Annular Pancreas: abnormal Rotation of ventral bud forms a ring of pancreatic tissue that encircles 2nd part of duodenum presents with vomiting.

Derivatives of Mesogastrium

Dorsal Mesogastrium	<ul style="list-style-type: none"> ○ Greater omentum -- (Gastrocolic, gastrosplenic, and Gastrophrenic Ligaments) ○ Splenorenal ligament, Phrenicocolic ligament ○ Mesentery of small Intestine, Mesoappendix. Transverse Mesocolon
Ventral Mesogastrium	<ul style="list-style-type: none"> ○ Lesser omentum -- (Hepatogastric and hepatoduodenal ligaments) ○ Falciform ligament, Coronary ligament (Right and left triangular ligaments)

	Gastroschisis	Omphalocele
Incidence	1 in 10,000 (now increasing)	1 in 5,000
Defect Location	Right paraumbilical	Central
Covering Sac	Absent	Present (unless sac ruptured)
Description	Free intestinal loops	Firm mass including bowel, liver, etc.
Association with Prematurity	50 % to 60 %	10% to 20%
Common associated Anomalies	Gastrointestinal (10% to 25%) Intestinal atresia, Malrotation Cryptorchidism (31%), Necrotizing enterocolitis (NE) - Common - 18%	Trisomy syndromes (30%) Cardiac defects(20%), Beckwith-Weidemann syndrome, Bladder extrophy, NE – Uncommon
Prognosis	Excellent for small defect	Varies with associated anomalies
Mortality	5% to 10%	(80% with cardiac defect)

OMPHALOCELE has O.O is closed letter so COVERING sac is present but covering sac is absent in Gastroschisis.

GENITOURINARY SYSTEM

Kidney Development: Three systems of kidney development are as follows:

1. Pronephric system	<ul style="list-style-type: none"> ❖ Appears at beginning of 4th week in cervical region Analogous to kidney of fish, Formed of tubules & a duct. ❖ Not functional in human and disappears.
2. Mesonephric system	<ul style="list-style-type: none"> ❖ appears at end of 4th week in thoracic & abdominal regions. ❖ Analogous to kidney of amphibians Formed of tubules & a duct. Functions temporarily. the duct in male forms genital duct and in both sexes forms ureteric bud
3. Metanephric system	<ul style="list-style-type: none"> ❖ Permanent Kidney. Appears at 5th week in pelvis. ❖ Starts to function at 9th week. Formed of 2 origins: ❖ Ureteric Bud: derived from mesonephric Duct → Gives Collecting part of Kidney. ❖ Metanephric Blastema (Mass) -- Derived from Nephrogenic cord It Gives Excretory part of Kidney.

Ureter, Pelvises, Calyces & Collecting System

- ❖ Ureteric bud arises as outgrowth of mesonephric duct gives rise to → Ureter, Pelvises, calyces.
- ❖ Collecting ducts fully canalized by 10th wk.
- ❖ Ureteric bud interacts with Metanephric mesenchyme/ cap to form → PCT, DCT, LOH, bowman capsule.

Urinary Bladder

- ❖ Epithelium of bladder is derived from both Endoderm + mesoderm.
- ❖ But for Trigone from Mesoderm. The urinary bladder is developed from 3 sources:
- ❖ **Vesicourethral canal (endoderm):** forms Major parts of the urinary bladder & prostatic urethra
- ❖ **Proximal part of allantois: (endoderm)** → apex of the Urinary bladder (the distal part of the Allantois gives Urachus – obliterated urachus → median Umbilical ligament)
- ❖ Absorbed proximal parts of Mesonephric ducts: (mesoderm) → the Trigone of urinary Bladder

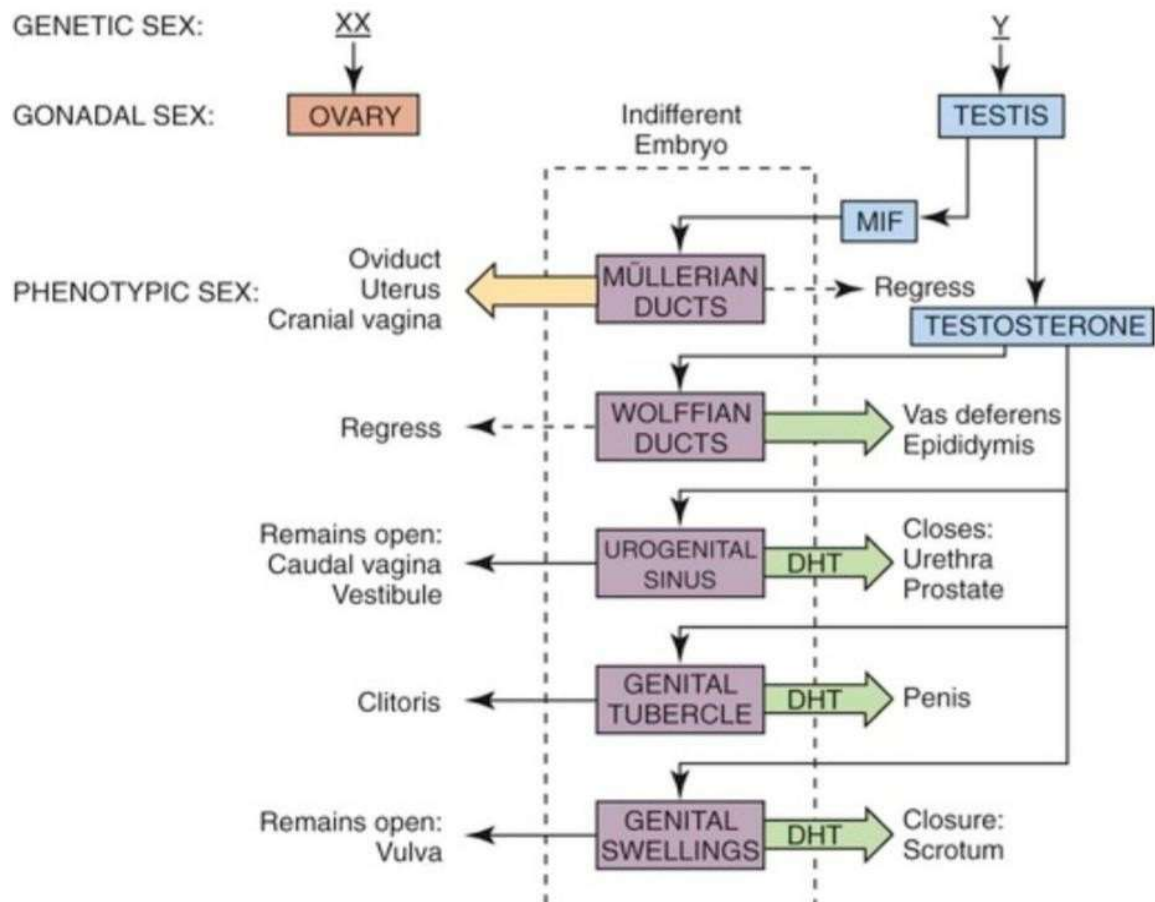
Vagina Development

- ❖ Upper part develops from Lower part of Paramesonephric duct.
- ❖ Lower Vagina is derived from Urogenital sinus.

Anomalies of Development of Genitourinary system

- ❖ **Duplication of ureter & collecting system:**
Occurs by early division of Ureteric Bud can give rise to double/bifid ureter. But alternatively, through 2 ureteric buds interacting with metanephric blastema can lead to development of duplex collecting system.
- ❖ **Pelvic Kidney:**
failure of ascent into abdomen. Evident as Shadow in the pelvic region
- ❖ **Horseshoe Kidney:**
Fusion of lower poles of kidney. Ascent prevented by Inferior mesenteric artery. May present with Hydronephrosis.
- ❖ **Renal Agenesis:**
Ureteric bud fails to induce differentiation of metanephric mesenchyme.
- ❖ **PUJ:**
It is last to canalize. Its obstruction is Most common cause of pathological pre-natal hydronephrosis.
- ❖ **Posterior urethral valves:**
Membrane remnant in posterior (prostatic) urethra can be diagnosed pre-natal by bilateral hydronephrosis (BCQ)
- ❖ **Bicornuate Uterus is associated with Renal anomalies.** (BCQ)

Embryonic Structure	Female	Male Homologue
Gonad	Ovary	Testis
Cortex	Ovarian Follicles	Seminiferous Tubules
Medulla	Rete Ovarii	Rete Testis
Gubernaculum	Ovarian Ligament Round Ligament of Uterus	Gubernaculum Testes or Scrotal Ligament
Mesonephric Tubules	Oophoron. Par Oophoron	Efferent Ductules
Mesonephric Duct/Wolffian Duct	Appendix Vasculosa Duct Of Oophoron, Duct of Gartner	Appendix Of Epididymis Duct Of Epididymis + Ductus Deferens Ejaculatory Duct, Seminal Vesicles
Paramesonephric / Müllerian Duct	Hydatid Of Morgagni Uterus + Uterine Tubes + Vagina	Appendix - Testis
Urogenital Sinus	Urethra, Vaginal Urethra Paraurethra I Glands Greater Vestibular Glands	Prostate + Prostatic Utricle, Urethra + Bulbourethral Glands
Sinus Tubercle	Hymen	Seminal Colliculus
Phallus	Clitoris	Penis
Urogenital Folds	Labia Minora	Ventral Aspect of Penis
Labioscrotal Swelling	Labia Majora	Scrotum



HISTOLOGY

(Microscopic Study of tissues)

FOUR BASIC TYPES OF TISSUES

Epithelial Tissue	Functions as covering layer + secretions e.g., Skin surface (epidermis) <u>Types Of Epithelia in Body:</u> <ul style="list-style-type: none">• Simple: Squamous, Columnar, Cuboidal and Pseudostratified Ciliated• Compound: Stratified Squamous Keratinized/ Dry, Stratified Squamous Non- Keratinized/ Moist type. Stratified Columnar, Stratified Cuboidal, Transitional epithelium or Urothelium that is dome shaped.				
ConnectiveTissue (C.T)	Functions: Support & Protection. Following types of C.T are there: <ul style="list-style-type: none">1. Specialized CT → Bone, Cartilage, Blood, and Lymph2. Proper C.T: It Is divided into Dense C.T & Loose C.T<ul style="list-style-type: none">i. Dense C.T → Elastic (Arteries), Regular (Tendon) ,Irregular (Epimysium & Perimysiumii. Loose CT: Areolar (Endomysium), Reticular (soft skeleton) and Adipose (Fat)				
Muscles	<ul style="list-style-type: none">• Striated → Cardiac and skeletal.• Non-striated → Smooth muscles• Cardiac and smooth muscles are involuntary whereas skeletal muscles are voluntary.• Skeletal muscles have: an Origin (fixed part – no movement) , fleshy belly and, an insertion (mobile part)• Tendon is a type of dense C.T that connects bone to muscle (TBM)• Ligament is a type of dense C.T --connects bone to bone. <p style="text-align: center;"><u>Coverings of Muscle</u></p> <table border="1"><tr><td>• Epimysium, Perimysium and Endomysium</td></tr><tr><td>• Epimysium -- layer of C.T that covers entire muscle.</td></tr><tr><td>• Perimysium – a layer of C.T that covers a muscle fascicle/bundle.</td></tr><tr><td>• Endomysium -- layer of C.T that covers individual muscle fibers</td></tr></table>	• Epimysium, Perimysium and Endomysium	• Epimysium -- layer of C.T that covers entire muscle.	• Perimysium – a layer of C.T that covers a muscle fascicle/bundle.	• Endomysium -- layer of C.T that covers individual muscle fibers
• Epimysium, Perimysium and Endomysium					
• Epimysium -- layer of C.T that covers entire muscle.					
• Perimysium – a layer of C.T that covers a muscle fascicle/bundle.					
• Endomysium -- layer of C.T that covers individual muscle fibers					
Nervous Tissue	For communication Brain, Spinal cord, and Nerves -- discussed in Neuro section.				

TWO BASIC TYPES OF ORGANS

Solid Organs	<p>Solid Organs have 2 parts.</p> <ol style="list-style-type: none"> 1. Stroma -- gives rise to Capsule. 2. Parenchyma -- main functional or structural mass of an organ. <p>Examples of solid organs are Lymph node, Liver and Lung etc.</p>
Hollow Organs	<p>They are Like Tube- shaped and Have g 4 layers as follows -- From Inner to Outer:</p> <ol style="list-style-type: none"> 1. Mucosa – innermost layer 2. Submucosa – strongest layer of bowel / GIT , it contains Meissner’s plexus (controls secretions and blood flow). 3. Muscularis Externa -contains Myenteric plexus which is responsible for Gut movements. 4. Serosa/ Adventitia : (Serosa is lined by Mesothelium – derivative of Mesoderm) <ul style="list-style-type: none"> ○ Submucosa Contains Abundant glands. ○ Abundant glands in Oral Cavity present in Submucosa > Lamina Propria. ○ Location of esophageal varices is Submucosa. ○ Gall bladder Lacks Submucosa & Muscularis Mucosa. ○ In GIT outer longitudinal and inner circular layer of smooth muscles is present in Muscularis mucosae. ○ Muscularis mucosa is involved in Mega colon/Hirschsprung’s disease. ○ Serosa is Presented where Tube pass from Body cavities e.g., Stomach. ○ Adventitia is present where tube pass through Body walls e.g., esophagus.

1. EPITHELIAL TISSUE

GIT, Glands & Accessory Git Organs

GIT is a hollow Organ (Mucosa, Submucosa, M. Mucosa & Serosa/Adventitia)

Salivary Glands: (3 Main + Numerous minors)

- Epithelium of Main Lining ducts of Salivary glands is **Stratified Columnar**
- Sweat glands have Both Sympathetic & Parasympathetic supply.
- Which of following tissue/organ has dual autonomic supply, but not reciprocal action?

Ans: Salivary gland Because **both INC secretions of salivary glands. Therefore, no reciprocal action.**

SALIVARY GLANDS	
Parotid Gland	<ul style="list-style-type: none"> ○ Produces Chiefly Serous nature saliva and Serous Acini mainly present. ○ Epithelium: Main Ducts lined by Stratified columnar and Small intercalated ducts lined by simple low cuboidal. ○ Parotid Duct (Stensen Duct) Pierces buccinator and moves from buccal space to open in the mouth opposite 2nd Upper Molar
Submandibular Gland	<ul style="list-style-type: none"> ○ Produces Predominantly Mixed nature saliva (Serous & Mucinous). ○ Lined by Mixed Serous & Mucinous acini but Predominantly more Serous > Mucinous. ○ Duct Of Gland (Wharton's Duct) opens in sublingual Caruncle at the Lateral sides of Frenulum of tongue in the floor of mouth
Sublingual Gland	<ul style="list-style-type: none"> ○ Produces Mucinous saliva. ○ Contains Abundant Mucinous and very small no. Of Serous Acini. ○ Duct Opens at floor of mouth in sublingual caruncle near submandibular gland.
SWEAT GLANDS	
Features	<ul style="list-style-type: none"> ○ Lined by Stratified Cuboidal > Stratified Columnar (may have both) ○ Sweat glands are Coiled Tubular Structure ○ Three types of sweat glands as given below
Eccrine Glands	<ul style="list-style-type: none"> ○ Abundant all over body, especially Palms. ○ They are independent of hair follicle, hence, called atrichial. ○ Secretions are Salty and contain Ammonia & Urea etc.
Apocrine Glands	<ul style="list-style-type: none"> ○ Present in Groins + Axilla ○ (Secretions containing more Fat) Dependent on Hair follicles. (Epitrichial) ○ Remember: Breast is a modified Apocrine Sweat gland and Stratified Cuboidal lines the ducts.
Mixed glands	<ul style="list-style-type: none"> ○ Mixed /Apo eccrine Develop from eccrine like precursors.

ORAL CAVITY & GIT ORGANS	
Stratified Squamous Keratinized (Dry)	<ul style="list-style-type: none"> Outer Lips, Dorsum Tongue , Gingiva and Anus Below Hilton Line
Stratified Squamous Non- Keratinized (moist)	<ul style="list-style-type: none"> Inner Lips, Mouth , Oropharynx, Soft palate, filiform papillae (taste buds) , Pharynx, Oesophagus + Anus Above Hilton line.
Simple Columnar	<ul style="list-style-type: none"> Simple Columnar Non-Ciliated present on : Stomach, Small & Large intestines, Rectum Simple Columnar + Microvilli : Gallbladder Gallbladder has extensive Mucosal folds, No submucosa and no Muscularis mucosa. Payer patches present in Ileum. Haustrations make Intestine look Like Vertebrae. Appendix has no Taenia Coli.
Taste Buds	<ul style="list-style-type: none"> Filiform Papillae : No Taste Buds Present but Most Numerous & Smallest Foliate Papillae are Rudimentary. Circumvallate Papillae are Present Near Posterior 1/3rd Tongue and Contain von Ebner Glands. Von Ebner Glands Secrete Lingual Lipase. Fungiform papillae : mushroom shaped. Receptors For Taste: Sweet at Tip of Tongue and Salty at Lateral Surfaces of Tongue Sour: From Behind Tip to Sides of Tongue) Umami Taste: Meat, Burgers Etc. and use glutamate as neurotransmitter
LIVER	<ul style="list-style-type: none"> Liver Is Surrounded by GLISON's Capsule and has 1.5 Kg Weight Major Function Is Metabolism, Detoxification, Urea Cycle and Clotting Factors Synthesis. Contains Sinusoids: A Type of Discontinuous Capillaries Kupffer Cells Are Macrophages Help in Immunity. Liver Does NOT Synthesize Gamma Globulins (They are Synthesized in Spleen by plasma cells). (BCQ) Functional Unit of Liver → Haptic Acinus, Remember it like: FA = Functional Acinus Structural Unit of Liver → Hepatic Lobule Now Learn the difference b/w Hepatic Lobule Vs Portal Lobule and Hepatic Acinus
Portal Lobule	<ul style="list-style-type: none"> It has Portal Triad in the Centre. Centrilobular Vein At the Periphery/Corners
Hepatic Lobule	<ul style="list-style-type: none"> Hexagonal shaped.(H for Hepatic & Hexagonal) Centrilobular Vein At Centre and Portal Triad at Periphery
Hepatic Acinus	<ul style="list-style-type: none"> Terminal hepatic veins at periphery and small portal tracts at centre. Hepatic Acinus Divided into 3 zones. 1. Zone I (Peri-Portal) : Around Portal Vein, Richly Oxygenated. Viral Hepatitis Occurs here. 2. Zone II (Intermediate) : Yellow Fever Zone. 3. Zone III (Centrilobular): Poorly Oxygenated and Drugs Metabolism (Xenobiotic) occurs.

RESPIRATORY SYSTEM	
❖	Pseudostratified Ciliated Columnar is the Main Epithelium.
❖	It is Present in Nose + Nasopharynx + Larynx, Trachea, Bronchi and False Vocal Cords
❖	True Vocal Cords: Stratified Squamous Non-Keratinized
❖	Nasal Vestibule: Stratified Squamous Keratinized (Dry)
❖	Simple Columnar in Pre- Terminal Bronchioles
❖	Simple Cuboidal: Terminal Bronchioles + Respiratory Bronchioles, Alveolar Ducts, and alveolar Sacs
❖	Alveoli Have Simple Squamous epithelium (For Gas Exchange)
❖	Smallest Diameter: Alveolus, Not Alveolar Duct/ Sac.
❖	Ground Substance of Alveolar Duct Is: Alveoli.
❖	Ground Substance of Alveoli Is Basement Membrane
❖	Goblet Cells -- Abundant in Bronchi & Tertiary Bronchus
❖	Clara Cells -- Numerous in Terminal Bronchioles.
❖	Intra Alveolar Cells Are Pneumocytes (Type 1 and type 2)
❖	Type 2 Pneumocytes produce Surfactant.
❖	Respiratory Zone of Lungs Have Type 1 Cells
❖	Cells Abundant in Inter-Alveolar Septum: Macrophages
❖	Pseudo Str Epithelium Has All Cells Present at Same Level at Base (Nuclei Lie at Different Levels)
❖	Chronic Rhinitis increases Goblet/ Mucous Cells
❖	Mucous Glands Present in Nose + Trachea.
❖	Lower Airways Don't Have Mucous Glands
❖	Trachea Is Formed by C Shaped Incomplete Cartilages (Hyaline)
❖	Auditory Tube or Eustachian Tube has: Pseudostratified Ciliated columnar epithelium.

GENITOURINARY SYSTEM	
Urinary System	<ul style="list-style-type: none"> ○ Main Lining Epithelium: Transitional (Urothelium) ○ Dome Shaped, Changes Shape and Flexible. ○ Present On Renal Calyces and Pelvis, Ureter, Bladder, Prostatic Urethra ○ Membranous + Penile Urethra has : Pseudostratified Non-Ciliated > Stratified Squamous Non-Keratinized. ○ Female Urethra Has Stratified Squamous Non-Keratinized. ○ PCT + DCT → Simple Cuboidal with Microvilli. PCT + DCT are Present in Cortex. ○ PCT Has Abundant Microvilli Than DCT ○ Loop of Henle → Present in Medulla and lined by Simple Squamous epithelium. ○ Parietal Layer of Bowman's Capsule Has Simple Squamous Epithelium ○ Visceral Layer OF Bowman's CAPSULE Has Podocytes ○ Bowman's Capsule Modifies Its Lining Epithelium. ○ Collecting Ducts are lined by Simple Cuboidal > Simple Columnar ○ Collecting Ducts Converge into Medullary Rays That Form Renal Papillae ○ Medullary Rays Contain Blood Vessels, Collecting Ducts and Straight Portion of Nephrons. Location Of Medullary Rays is Renal Cortex. ○ Renal Columns are Extensions of Cortex Present in Renal Medulla ○ Minor Calyces Receive Urine from Renal Papillae ○ Collecting Tubules Are Not Part of Nephron ○ Regarding Macula Densa: Flat Cells > Deep Basal Lamina ○ If Above Options Are Not Present, then choose Tall Cells Having Prominent Nuclei & Scattered Mitochondria in Periphery. They Are Linked to DCT Not PCT. ○ Don't Choose Flat Epithelium / PCT, Because They Are Flat, Elongated Cells, Not Flat Epithelium

Reproductive System

MALE

- ✚ TESTIS has 3 layers from INNER to OUTER as :
- ✚ Tunica Vaginalis, Tunica Albuginea and Tunica Vasculosa (Innermost).
- ✚ Tunica Vaginalis is derived from Parietal Peritoneum.
It has 2 layers serous and visceral.
- ✚ Fluid accumulates in b/w Serous & Visceral Layers of T. Vaginalis
- ✚ Needle must NOT Pierce T. Albuginea while draining Fluid (Hydrocele) etc.
- ✚ Dartos fascia consists of Smooth Muscles only.

- | | |
|---|---|
| <ol style="list-style-type: none"> 1. Prostate 2. Seminal Vesicles 3. Epididymis 4. Ductus Deferens | Pseudostratified non-ciliated
epithelium is present in all these. |
|---|---|

- ✚ Ejaculatory Duct has Simple Columnar type.
- ✚ Seminiferous Tubules have Stratified Cuboidal lining.
- ✚ Epididymis Has Sterco Cilia
- ✚ Ductus Deferens Has Thick Muscular Wall + Pseudostratified Epithelium.
- ✚ Prostate has Abundant Fibromuscular Stroma and Abundant Acini
- ✚ Corpora Amylacea: Extracellular, Eosinophilic amyloid bodies or concretions present in Prostate adjacent to damaged Epithelium.
- ✚ Seminal Fluid has abundant Fructose.

FEMALE

- ✚ Ovary has Simple Cuboidal. While Developing Follicle Has Stratified Cuboidal
- ✚ Uterus → Simple Columnar + CRYPTS + indistinct layer of smooth muscles
- ✚ Uterine Tubes/ Fallopian Tubes → Simple Col Ciliated + Clefts
- ✚ Remember It by **F** In **F**allopian & **C**lefts Whereas **T** In **C**rypts & **U**terus.
- ✚ Endo Cervix → Simple Columnar with Indistinct Layer of Muscles
- ✚ Ecto Cervix + Vagina → Stratified Squamous NON-Keratinized
- ✚ Lamina Propria of Vagina Has Abundant Elastic Tissue Only

2. CONNECTIVE TISSUE

Blood	<ul style="list-style-type: none">A type of specialized connective tissue, Acts as a Buffer, Fluid of Life -- 5 Litre Normal Vol.Blood consists of:<ul style="list-style-type: none">a) 55 % plasma (mainly water)b) 45% formed elements (RBCs, WBCs, and Platelets)Haematocrit or packed cell volume consists of RBCs only.Buffy coat consists of WBCs and platelets			
Bone	<ul style="list-style-type: none">A specialized C.T having 2 types as follows:Compact Bone: Outer layer made of Osteons.Spongy Bone: inner cancellous layer made of Trabeculae. It has Bone marrow.Covering of the Bone is called periosteum.In Fracture Periosteal Cells Grow that Starts Healing <p><u>Cells of bone:</u></p> <table><tr><td><ul style="list-style-type: none">Osteoblasts : Bone Forming, inc ALP</td></tr><tr><td><ul style="list-style-type: none">Osteocytes: Mature bone cells derived from Osteoblasts, lie in Lacuna.They maintain bone integrity.</td></tr><tr><td><ul style="list-style-type: none">Osteoclasts: bone resorption cells. Located in shallow grooves called Howship Lacunae.</td></tr></table> <ul style="list-style-type: none">Bone Remodelling is done By Both Osteoblasts + Osteoclasts.Bone Regeneration is done by Vit C (as Vit C helps in collagen formation).Bone Mineralization is done by Vit D (For strong bones)Circumferential Lamellae Around Central Canal Form Osteon.Osteon Is Unmineralized Bone MatrixOsteoporosis Is Due to Increase Osteon Maturation Time.	<ul style="list-style-type: none">Osteoblasts : Bone Forming, inc ALP	<ul style="list-style-type: none">Osteocytes: Mature bone cells derived from Osteoblasts, lie in Lacuna.They maintain bone integrity.	<ul style="list-style-type: none">Osteoclasts: bone resorption cells. Located in shallow grooves called Howship Lacunae.
<ul style="list-style-type: none">Osteoblasts : Bone Forming, inc ALP				
<ul style="list-style-type: none">Osteocytes: Mature bone cells derived from Osteoblasts, lie in Lacuna.They maintain bone integrity.				
<ul style="list-style-type: none">Osteoclasts: bone resorption cells. Located in shallow grooves called Howship Lacunae.				
Cartilage	<p><u>Hyaline:</u> Fibres Not Visible, Glass Like Appearance and Most Abundant Type. It is Present On:</p> <ul style="list-style-type: none">Thyroid, Cricoid, Arytenoid, Nasal, Epiphyseal Cartilage of Long Bones, Ribs (Costal Cartilage) <p><u>Fibrocartilage:</u> Type 1 Collagen, Fibres Visible and Present on Midline Joints.</p> <ul style="list-style-type: none">Intervertebral Disc, Glenoid Labarum, Knee Menisci, Pubic Symphysis and Manubriosternal Joint <p><u>Elastic:</u> Type 2 Collagen Like Hyaline but Fibres are Visible. It is Present On (All E's): Ear Pinna, External Auditory Meatus and Epiglottis</p>			
Vessels	<ul style="list-style-type: none">layers as Tunica Intima (Innermost), Tunica Media (Middle) and Tunica Adventitia (Outermost) Endothelium Lining Is Simple Squamous (Also, lines Lymphatics)Pericytes Are Present Around Vessels (Especially Medium Sized Vessels) <p><u>TYPES OF ARTERIES</u></p> <ul style="list-style-type: none">Elastic Arteries: Large arteries, contain more elastic fibres and less smooth muscles in tunica media.Muscular Arteries: Medium sized arteries, 0.5 - 10mm diameter and have More smooth muscles and less elastic fibres in media. <p><u>TYPES OF VEINS:</u></p> <ul style="list-style-type: none">Large sized, Medium sized and Small sizedVeins have same three layers as arteries. May or may not have valves.			

ENDOCRINE GLANDS	
Pituitary Gland	<ul style="list-style-type: none"> Five types of cells present in anterior pituitary gland as follows: Somatotropes: 50 % of cells, acidophilic or eosinophilic that secrete growth hormones . Lactotropes: 10 – 30 % of cells, acidophilic -- secrete prolactin. Corticotropes: 10 % of cells, chromophobes or pale staining and secrete ACTH. Thyrotropes: 5 % of cells, Basophilic + secrete TSH. Gonadotropes: 20 % of cells, Weakly basophilic and secrete FSH and LH.
Thyroid Gland	<ul style="list-style-type: none"> Epithelium Changes Shape According to Gland Activity Inactive State → Simple Cuboidal. Active State → Simple Columnar If Active/ Non-Active Not Mentioned in Exam : Prefer Simple Cuboidal Follicular cells are abundant in thyroid gland that contain colloid. Parafollicular cells secrete calcitonin. (Tumor marker of medullary thyroid CA is calcitonin).
Parathyroid Gland	<ul style="list-style-type: none"> They contain two types of cells. Chief cells or principal cells: Polygonal shaped + produce PTH Oxyphil cells: produce PTHrP and calcitonin. They Stain Eosinophilic on H & E Stain.
Adrenal Gland	<ul style="list-style-type: none"> Adrenal Cortex 3 Layers : Zona Glomerulosa, Zona Fasciculata and Zona Reticularis Adrenal Medulla Contains Entero-Chromaffin Cells. Tight Cells in Adrenal Medulla are Lined by Mesothelium Mesothelium is Simple Squamous epithelium (Also lines Pericardium, Pleura, Peritoneum)

COLLAGEN

- Most Abundant Protein in Body, While Most Abundant Inside the Cell is Actin
- Up till Now Around 30 Approx. Types Discovered but Major Are 4 Types as Follows:
- As The Number Goes High -- the Strength Decreases (Weaker).

Type 1 collagen	Bone > Skin, Tendons, Fibrocartilage Late Wound Healing
Type 2 collagen	Cartilage (Hyaline Mainly); Nucleus Pulposus.
Type 3 collagen	Blood Vessels, Uterus, Early Wound Healing , Reticular Fibres, Hypertrophic Scar. Keloid, Fetal Tissue
Type 4 collagen	Basement Membrane , Basal Lamina, Lens

Tonsils & Conjunctiva

- Tubal + Pharyngeal (Adenoids) Tonsils Have Pseudostratified Ciliated Epithelium
- Palatine + Lingual have Stratified Squamous Epithelium
- Conjunctiva Stratified Columnar > Stratified Squamous Non-Keratinized
- Cornea: Stratified Squamous Non-Keratinized.
- Pacinian Corpuscles Are Not Part of Epidermis (As They Are in Deep Dermis)
- Lymphatic tissue + Stratified Squamous Epithelium → **Palatine** Tonsils
- Lymphoid tissue + Simple Cuboidal: Payer's Patches
- True epithelium does not present in Inter articular joint spaces.
- Type 1 Synoviocytes make Joint fluid.

GENERAL ANATOMY

- The study of general body structures (skin, Bone, muscle, joints) is known as general anatomy.
- While gross anatomy is describing body components based on Dissection & Observation
- Anatomical planes divide body into Right / Left, Superior / inferior and Anterior / posterior halves.

Coronal Plane	<ul style="list-style-type: none"> ○ Divides the Body into Anterior and Posterior Parts (Remember -- CAP) ○ Ventral Cavity: Thoracic, Abdomen & Pelvis ○ Dorsal Cavity: Cranial (Brain) + Spinal Cord ○ Adduction & Abduction occur at this Plane
Sagittal Plane	○ Divides Body into Left and Right Halves. Flexion + Extension occurs at Sagittal Plane
Transverse Plane	○ Also known as axial /horizontal plane that divides the body into superior & inferior parts.

SKIN

- It is the largest organ and 1st line of defence as well.
- Type 1 collagen is present in skin. Skin has 3 parts: Superficial epidermis, deep dermis + Hypodermis.

Superficial Epidermis	<ul style="list-style-type: none"> • Waterproof barrier and Outermost layer. • Layers of Epidermis: Remember → COME Let's Get Sunburned. • Stratum Corneum (outer), Lucidum, Granulosum, Spinosum and Basale (deepest) • Stratum Basale + Spinosum are called germinativum. • Key Facts regarding Layers • Location of Melanocytes is Stratum Basale of Epidermis. • Active Mitosis occurs in Basale layer. • In Acanthosis Stratum Spinosum is involved • Langerhans cells /Skin Histocytes (Macrophages) -- numerous in Stratum Spinosum. • Corneum contains soft keratin, dead cells + Soft Keratin and, Shed off regularly. • Stratum Lucidum composition is not same throughout the body. • It is different on palm & soles
Deep Dermis	<ul style="list-style-type: none"> • Gives cushion effect, Sensations and contains vessels. It has 2 layers. • Both have Collagen + elastic fibres. • Papillary Layer: contains blood vessels that also help regulate body temperature. It is immediately below Epidermis. • Reticular Layer: deeper layer of dermis, contains Sweat glands, Sebaceous gland + nerve endings • Reticular Fibres present more in Tonsils than Dermis. Tonsils > Dermis • Preganglionic are type B fibres and myelinated. post ganglionic are Unmyelinated TYPE C fibres
Hypodermis	<ul style="list-style-type: none"> • Also known as: Superficial Fascia or Deep Subcutaneous Layer • Made of FAT & Loose areolar connective tissue • Fascia is of 2 types; superficial and Deep fascia • Superficial fascia as described here is simply hypodermis while; • deep fascia is fibrous tissue covering Muscles and tendons

SKIN APPENDAGES

Glands (Sweat + Sebaceous), Hair Follicles, Hair & Nails.

Glands	<ul style="list-style-type: none"> • Sweat Glands: Present all over the skin. Greatest on palm & soles. But NOT present on the Tympanic Membrane, lips margins, glans penis & Labia minora • Sebaceous Glands: derived from root of Hair Follicle. They Pour sebum onto Shafts of hairs & open on Hairless skin of Lips, Nipples, Prepuce, Glans penis & Labia Minora • Sebaceous Cysts occur mostly on Scalp. • Palms & soles do not contain sebaceous glands.
---------------	--

	<p>Remember</p> <ul style="list-style-type: none"> Sweat glands are abundant on palm & soles. Sebaceous glands are absent on palm & soles. On Lips, Glans penis & Labia minora: sebaceous glands are more and sweat glands are absent. Mucous glands are not skin appendages
Hairs & Hair follicles	<ul style="list-style-type: none"> Hair shaft is made of 3 layers : cuticle, cortex, and medulla. Main mass/ bulk of hair shaft is due to cortex Boil is infection of hair follicle caused by commonly s. aureus (1 cm red tender papule/nodule) Carbuncle is inf of several hair follicles mostly on nape of neck (in diabetics). Red plaque seen of several cm Contraction of erector pili (smooth muscles) called goosebumps due to shivering, fright & horror. Supplied by sympathetic fibres Partial thickness burns heal from hair follicles, glands, and cells of edges of burns A burn deeper than Sweat glands heals Slowly and only from edges.
Nail	<ul style="list-style-type: none"> Hard Keratin or End Hard Keratin is present in Nails.

BONES							
<ul style="list-style-type: none"> Bone is a Specialized Connective Tissue that has Type 1 Collagen). Total bones are 300 at Birth; 206 in adults. Main mineral of Bone is Calcium Hydroxyapatite Crystals. (BCQ). Calcium Carbonate is main Buffer. The Cover of Bone is Periosteum. It Forms majority of New Bone after Fracture (BCQ) What about Bone is True: Appositional growth (growth in Width) (BCQ) Circumferential lamellae Form Osteon around the central canal. Cementum is an Avascular bone like Tissue covers Tooth surface. Receives Blood from Periodontal Ligament, while bone is Vascular. 							
TYPES OF BONE	FEATURES						
Long bones	<p>Length > Breadth, e.g. Clavicle, Humerus, Ulna, Radius, Femur & Tibia.</p> <p>Part of Long Bones</p> <table> <tr> <td>Diaphysis or Shaft</td><td> <ul style="list-style-type: none"> Ossifies from Primary Centre Site of Ewing Sarcoma is diaphysis. Central marrow cavity is lined by Endosteum. Circumferential Lamina are arranged regularly around central canal. Osteonic canal Running Obliquely & transversely connecting Medullary cavity with Cortex is the Volkmann canal </td></tr> <tr> <td>Metaphysis</td><td> <ul style="list-style-type: none"> The ends of active growing Diaphysis Near Epiphysis Nutrient artery to Long Bone passes through Metaphysis. Both Ends of Long Bones are Supplied by Epiphyseal Arteries. In Osteomyelitis hematogenous spread occurs by Metaphysis. Site of Osteosarcoma is Metaphysis </td></tr> <tr> <td>Epiphysis</td><td> <ul style="list-style-type: none"> Ends of Bones that Ossify from Secondary center of Ossification. Site of Giant cell tumor (Soap bubble lesion) is epiphysis. Linear Growth is affected in Epiphyseal Cartilage /Plate fracture. Remnant of Epiphyseal Cartilage is Epiphyseal line. Epiphyseal Plate is seen post-Partum to determine Puberty. Epiphysis of GIRLS close Earlier than Boys by difference of 3 Years </td></tr> </table>	Diaphysis or Shaft	<ul style="list-style-type: none"> Ossifies from Primary Centre Site of Ewing Sarcoma is diaphysis. Central marrow cavity is lined by Endosteum. Circumferential Lamina are arranged regularly around central canal. Osteonic canal Running Obliquely & transversely connecting Medullary cavity with Cortex is the Volkmann canal 	Metaphysis	<ul style="list-style-type: none"> The ends of active growing Diaphysis Near Epiphysis Nutrient artery to Long Bone passes through Metaphysis. Both Ends of Long Bones are Supplied by Epiphyseal Arteries. In Osteomyelitis hematogenous spread occurs by Metaphysis. Site of Osteosarcoma is Metaphysis 	Epiphysis	<ul style="list-style-type: none"> Ends of Bones that Ossify from Secondary center of Ossification. Site of Giant cell tumor (Soap bubble lesion) is epiphysis. Linear Growth is affected in Epiphyseal Cartilage /Plate fracture. Remnant of Epiphyseal Cartilage is Epiphyseal line. Epiphyseal Plate is seen post-Partum to determine Puberty. Epiphysis of GIRLS close Earlier than Boys by difference of 3 Years
Diaphysis or Shaft	<ul style="list-style-type: none"> Ossifies from Primary Centre Site of Ewing Sarcoma is diaphysis. Central marrow cavity is lined by Endosteum. Circumferential Lamina are arranged regularly around central canal. Osteonic canal Running Obliquely & transversely connecting Medullary cavity with Cortex is the Volkmann canal 						
Metaphysis	<ul style="list-style-type: none"> The ends of active growing Diaphysis Near Epiphysis Nutrient artery to Long Bone passes through Metaphysis. Both Ends of Long Bones are Supplied by Epiphyseal Arteries. In Osteomyelitis hematogenous spread occurs by Metaphysis. Site of Osteosarcoma is Metaphysis 						
Epiphysis	<ul style="list-style-type: none"> Ends of Bones that Ossify from Secondary center of Ossification. Site of Giant cell tumor (Soap bubble lesion) is epiphysis. Linear Growth is affected in Epiphyseal Cartilage /Plate fracture. Remnant of Epiphyseal Cartilage is Epiphyseal line. Epiphyseal Plate is seen post-Partum to determine Puberty. Epiphysis of GIRLS close Earlier than Boys by difference of 3 Years 						
Short bones	<ul style="list-style-type: none"> Length = Width, Cuboidal in shape. E.g. 7 Tarsals & 8 Carpals 						
Long short bones	<ul style="list-style-type: none"> Metatarsal & Metacarpals 						
Irregular bones	<ul style="list-style-type: none"> Complicated shape; HIP bone, Vertebrae, Zygomatic, Ear Ossicles (BCQ) 						
Flat bones	<ul style="list-style-type: none"> Facial Bones mainly: Frontal, Maxillary, Ethmoid, sphenoid (BCQ) Make Skull Lighter. 						
Pneumatic bones	<ul style="list-style-type: none"> Scapula, Skull, Sternum & Ribs. Sternum contains Significant Red Marrow in adults 						
Sesamoid bones	<ul style="list-style-type: none"> Reduce Friction, round bone formed in Tendons. Patella is Largest Sesamoid Bone Ala Of Nose > Larynx is Sesamoid Cartilage (BCQ). Examples of sesamoid bones are: Pisiform in Flexor Carpi Ulnaris. Riders Bone in Adductor Longus Fabella (Not Fibula) in lateral Head of Gastrocnemius. 						
Accessory bones	<ul style="list-style-type: none"> Cervical Rib (Attached at C8 Vertebrae but compresses T1 segment (BCQ) 						



BONE DEVELOPMENT OR OSSIFICATION		
Centres of ossification	Primary center	<ul style="list-style-type: none"> Present In Diaphysis Appears 8th week of Intrauterine to 10 weeks after Birth.
	Secondary center	<ul style="list-style-type: none"> In Epiphysis at the age of 1 to 2 yrs. Remember it like: D comes before E. So, D/Diaphysis is Primary before E/Epiphysis (2ndary) Exception is the Distal End of Femur, here, the 2ndry centre is present at Birth.
Types of ossifications	Primarily two types of ossifications: endochondral and intramembranous ossification	
	Endochondral	<ul style="list-style-type: none"> Hyaline Cartilage serves as Model that is later replaced by Bone. <u>Examples:</u> All long Bones (except Clavicle), Short Bones, Irregular Bones, Ethmoid, Inferior Concha
	Intramembranous	<ul style="list-style-type: none"> No Cartilage involved and Mesenchymal Tissue laid bone by Osteoblasts. <u>Examples</u> Clavicle, Facial Bones, Maxilla, Zygomatic, Nasal, Vomer and Lacrimal bones, Vault of Skull (Frontal + parietal), Sub periosteal Bones. In Parietal Bone, Angle is last to Ossify
	Membrano-cartilaginous	<ul style="list-style-type: none"> These bones ossify by both ways. Mnemonics = MOST <u>Mandible</u>, Occipital, Temporal, <u>Sphenoid</u>
Ossification time of bones (imp)	<ul style="list-style-type: none"> ➤ 1st Bone to ossify in Intrauterine life is Clavicle. ➤ Capitulum – 01 Years ➤ Radial Head – 03 years ➤ Medial Epicondyle – 05 years ➤ Trochlea – 07 years ➤ Olecranon – 09 years, ➤ Lateral Epicondyle – 11 years (BCQ) ➤ Remember these by: C1, R3, M5, T7, O9, L 11 	

BONE MARKINGS	
Fovea	Small Pit/Pinpoint depression on Head of Bone (BCQ)
Fossa	Hollow or Depressed area
Groove	Elongated Depression
Crest & Tubercle	Crest = Ridge of bone while Tubercle = small, raised eminence
Capitulum & Tuberosity	Capitulum = Small, Round, Articular head while Tuberosity = large Round Elevation
Notch	indentation at the edge of bone

Digits abnormalities	✚ Polydactyly is extra digits/Supernumerary.
	✚ Brachydactyly is Shortening of fingers and Toes (BCQ).
	✚ Syndactyly is fusion of digits.
	✚ Ectrodactyly is absence of central digits of Feet/Hand
Reimplantation of digit	✚ Debridement → Bone Fixation → extensor repair → Flexor repair → Artery Repair → Nerve → Vein → Closure.
	✚ Structure to be Fixed 1 st is the Bone.

JOINTS

Union of 2 or more Bones is called joint Total joints = 360 approx. Types: FSC (Fibrous, Cartilaginous and Synovial)

Types	Features														
Fibrous joints	<p>Very Limited Movement as the articular surface are joined by fibrous tissue Types are: SSG.</p> <table> <tr> <td>Sutures</td><td> <ul style="list-style-type: none"> Aka Synarthrosis, Immovable, present in Skull. (S for Suture and Skull) </td></tr> <tr> <td>Gomphosis</td><td> <ul style="list-style-type: none"> Teeth & Sockets: Maxilla & Mandible Joints. (Gum for teeth's so, Gomphosis) </td></tr> <tr> <td>Syndesmosis Or Amphiarthrosis</td><td> <ul style="list-style-type: none"> Slight movement possible at these Joints and bones connected by Interosseous Membrane. Examples are Distal Tibiofibular Joints + Middle Radioulnar Joint </td></tr> </table>	Sutures	<ul style="list-style-type: none"> Aka Synarthrosis, Immovable, present in Skull. (S for Suture and Skull) 	Gomphosis	<ul style="list-style-type: none"> Teeth & Sockets: Maxilla & Mandible Joints. (Gum for teeth's so, Gomphosis) 	Syndesmosis Or Amphiarthrosis	<ul style="list-style-type: none"> Slight movement possible at these Joints and bones connected by Interosseous Membrane. Examples are Distal Tibiofibular Joints + Middle Radioulnar Joint 								
Sutures	<ul style="list-style-type: none"> Aka Synarthrosis, Immovable, present in Skull. (S for Suture and Skull) 														
Gomphosis	<ul style="list-style-type: none"> Teeth & Sockets: Maxilla & Mandible Joints. (Gum for teeth's so, Gomphosis) 														
Syndesmosis Or Amphiarthrosis	<ul style="list-style-type: none"> Slight movement possible at these Joints and bones connected by Interosseous Membrane. Examples are Distal Tibiofibular Joints + Middle Radioulnar Joint 														
Cartilaginous joints	<p>United by Cartilage. Types are as Primary and secondary Cartilaginous joints.</p> <table> <tr> <td>Primary cartilaginous Or Synchondrosis</td><td> <ul style="list-style-type: none"> Bones are United by Bar of Hyaline cartilage. No movement takes place or totally Immovable. Examples are: <ul style="list-style-type: none"> Present on the Union b/w epiphysis & Diaphysis , 1st Sterncostal Joints, Costochondral joints. Spheno-Occipital Joints, Developing Axial skeleton </td></tr> <tr> <td>Secondary cartilaginous Or Symphysis</td><td> <ul style="list-style-type: none"> United by Fibrocartilage (BCQ) They are Midline Joints e.g., <ul style="list-style-type: none"> Manubriosternal Joint, Intervertebral disc and Symphysis Pubis, also present between 2 Halves of Mandible at Birth (Symphysis Manti). </td></tr> </table>	Primary cartilaginous Or Synchondrosis	<ul style="list-style-type: none"> Bones are United by Bar of Hyaline cartilage. No movement takes place or totally Immovable. Examples are: <ul style="list-style-type: none"> Present on the Union b/w epiphysis & Diaphysis , 1st Sterncostal Joints, Costochondral joints. Spheno-Occipital Joints, Developing Axial skeleton 	Secondary cartilaginous Or Symphysis	<ul style="list-style-type: none"> United by Fibrocartilage (BCQ) They are Midline Joints e.g., <ul style="list-style-type: none"> Manubriosternal Joint, Intervertebral disc and Symphysis Pubis, also present between 2 Halves of Mandible at Birth (Symphysis Manti). 										
Primary cartilaginous Or Synchondrosis	<ul style="list-style-type: none"> Bones are United by Bar of Hyaline cartilage. No movement takes place or totally Immovable. Examples are: <ul style="list-style-type: none"> Present on the Union b/w epiphysis & Diaphysis , 1st Sterncostal Joints, Costochondral joints. Spheno-Occipital Joints, Developing Axial skeleton 														
Secondary cartilaginous Or Symphysis	<ul style="list-style-type: none"> United by Fibrocartilage (BCQ) They are Midline Joints e.g., <ul style="list-style-type: none"> Manubriosternal Joint, Intervertebral disc and Symphysis Pubis, also present between 2 Halves of Mandible at Birth (Symphysis Manti). 														
Synovial joints	<ul style="list-style-type: none"> Most Mobile and developed type of joints. Articular cartilage is Hyaline. Exceptions where the cartilage is fibrocartilage include: <ul style="list-style-type: none"> Temporomandibular, Acromioclavicular, Sternoclavicular joints. Synovial Joints have Synovial Cavity, Synovial Fluid, and synovial Membrane. Synovial Fluid is Secreted by Type 1 Synoviocytes (BCQ). True Epithelium is Not present at inter-Articular Joint spaces. Articular Disc is the oval plate of Fibrocartilage at knee and Sternoclavicular Joints. Stability Of Synovial Joints is Inversely to Mobility. Main factor for Stability is the Muscle Tone followed by Ligaments and Articular surfaces. <table> <tr> <th>Types</th><th>Examples</th></tr> <tr> <td>Ball & Socket</td><td> <ul style="list-style-type: none"> Circumduction Takes Place: Flexion, Extension, Adduction, Abduction. Like Bowling in Cricket & Swinging Arms Like Windmill's Is Circumduction Examples -- Hip Joint, Shoulder, Include-Stapedial Joints </td></tr> <tr> <td>Hinge</td><td> <ul style="list-style-type: none"> Elbow & Knee Joint. Knee Is the Most Complex Joint in Body. Joint at Knee Is Diarthrosis. </td></tr> <tr> <td>Pivot Joint or Trochoid</td><td> <ul style="list-style-type: none"> Proximal & Distal Radioulnar Atlanto-Axial: Movement of No (Head Nodding) While Crossing Road: Movement Of Neck Left & Right or Saying No Occurs at Pivot Joint </td></tr> <tr> <td>Ellipsoidal or Condylod</td><td> <ul style="list-style-type: none"> Wrist Joint and Metacarpophalangeal Joints Movement Of Saying Yes or Seeing Up/Down Takes Place at Biaxial Synovial Ellipsoidal Joints. </td></tr> <tr> <td>Saddle</td><td> <ul style="list-style-type: none"> Carpometacarpal Joints </td></tr> <tr> <td>Plane/ Gliding</td><td> <ul style="list-style-type: none"> Sacroiliac Joint Is Sometimes Described as Plane Synovial Type. </td></tr> </table>	Types	Examples	Ball & Socket	<ul style="list-style-type: none"> Circumduction Takes Place: Flexion, Extension, Adduction, Abduction. Like Bowling in Cricket & Swinging Arms Like Windmill's Is Circumduction Examples -- Hip Joint, Shoulder, Include-Stapedial Joints 	Hinge	<ul style="list-style-type: none"> Elbow & Knee Joint. Knee Is the Most Complex Joint in Body. Joint at Knee Is Diarthrosis. 	Pivot Joint or Trochoid	<ul style="list-style-type: none"> Proximal & Distal Radioulnar Atlanto-Axial: Movement of No (Head Nodding) While Crossing Road: Movement Of Neck Left & Right or Saying No Occurs at Pivot Joint 	Ellipsoidal or Condylod	<ul style="list-style-type: none"> Wrist Joint and Metacarpophalangeal Joints Movement Of Saying Yes or Seeing Up/Down Takes Place at Biaxial Synovial Ellipsoidal Joints. 	Saddle	<ul style="list-style-type: none"> Carpometacarpal Joints 	Plane/ Gliding	<ul style="list-style-type: none"> Sacroiliac Joint Is Sometimes Described as Plane Synovial Type.
Types	Examples														
Ball & Socket	<ul style="list-style-type: none"> Circumduction Takes Place: Flexion, Extension, Adduction, Abduction. Like Bowling in Cricket & Swinging Arms Like Windmill's Is Circumduction Examples -- Hip Joint, Shoulder, Include-Stapedial Joints 														
Hinge	<ul style="list-style-type: none"> Elbow & Knee Joint. Knee Is the Most Complex Joint in Body. Joint at Knee Is Diarthrosis. 														
Pivot Joint or Trochoid	<ul style="list-style-type: none"> Proximal & Distal Radioulnar Atlanto-Axial: Movement of No (Head Nodding) While Crossing Road: Movement Of Neck Left & Right or Saying No Occurs at Pivot Joint 														
Ellipsoidal or Condylod	<ul style="list-style-type: none"> Wrist Joint and Metacarpophalangeal Joints Movement Of Saying Yes or Seeing Up/Down Takes Place at Biaxial Synovial Ellipsoidal Joints. 														
Saddle	<ul style="list-style-type: none"> Carpometacarpal Joints 														
Plane/ Gliding	<ul style="list-style-type: none"> Sacroiliac Joint Is Sometimes Described as Plane Synovial Type. 														
Controversial BCQs	<ul style="list-style-type: none">  Cartilaginous + Amphiarthrosis = Costochondral Joint (Primary Cartilaginous type)  Fibrocartilaginous + Amphiarthrosis = Distal Tibiofibular > Manubriosternal  If Word Amphiarthrosis is not there; Then Distal Tibiofibular is Syndesmosis joint while Manubriosternal joint is the fibrocartilaginous type. 														

MUSCLES	
(Total muscles in human body are 640-650 approx.)	
Types	<ul style="list-style-type: none"> ○ Striated: Cardiac & Skeletal and NON-Striated: Smooth muscle ○ Smooth Muscles: ○ Slow & Sustained Contraction (BCQ), Uninucleated, Involuntary, present in GIT & Vessels. ○ Cardiac Muscles: Involuntary, intercalated disc present, Gap junctions, Uninucleated and rhythmic contractions ○ Skeletal Muscle: <ul style="list-style-type: none"> • Voluntary, rapidly contract and Multinucleated (BCQ) e.g., Limbs & Pharynx • Tendons attach Muscle to Bone while Ligaments are for Bone-to-Bone Attachment (BCQ) • Parts of skeletal muscles: origin, insertion, and belly • Origin: Least Movable Part while Insertion most mobile part • Belly is the Fleshy part of Muscle. Some Muscles have Fleshy belly Throughout (BCQ)
Classification of Skeletal Muscles Based on the Arrangement of Fibres	
Oblique muscle fibers	<p>Types: Triangular, Circular & Pennate Muscles.</p> <ul style="list-style-type: none"> i. Triangular: Pectoralis Major ii. Circular: Orbicularis Oris & Oculi iii. Pennate: Feather Like, fibers are arranged parallel to long axis of the bone. divided into 4 types further as follows: <ul style="list-style-type: none"> a. Unipennate e.g. Tibialis Posterior b. Bipennate e.g. Rectus Femoris c. Multipennate is the Strongest type e.g Deltoid (BCQ) d. Circumpennate e.g Tibialis Anterior
Parallel muscle fibers	<p>Types:</p> <ul style="list-style-type: none"> i. Fusiform: Biceps brachii (BCQ) ii. Quadrangular: Gluteus maximus. iii. Strap Muscles: Sartorius iv. Strap + tendinous Insertion: Rectus abdominis
Classification Based on the Action	
Prime Mover	Initiation + maintenance of movement e.g., Quadriceps in knee Extension
Antagonists	Oppose the action of Prime Mover. Biceps femoris Oppose Quadriceps action
Synergistic	Nullify the Unwanted effect of prime Mover e.g., Deltoid during abduction
Fixator	Stabilise the position of Joint to Prime Mover. E.g., Rotator cuff in Shoulder Abduction
Hybrid Muscles/Composite Muscles	
Having Dual Nerve Supply: Biceps femoris, Adductor Magnus, Pectineus, flexor digitorum Profundus, Pectoralis Major	

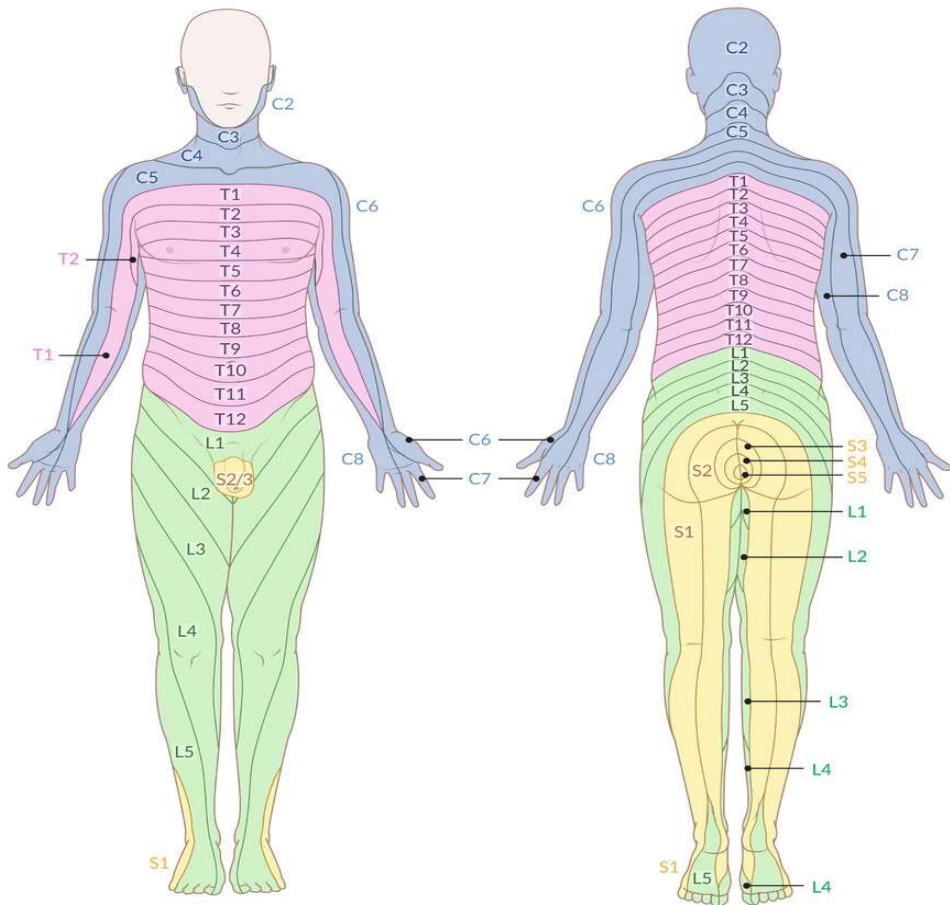
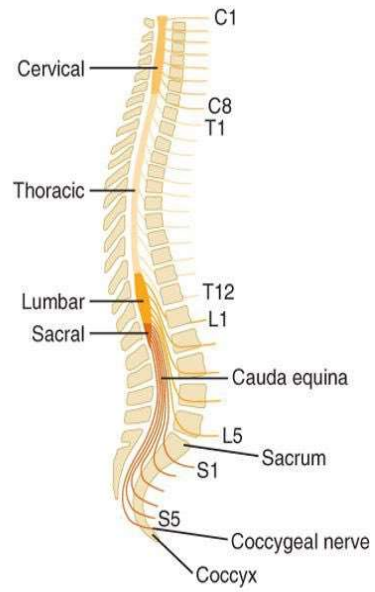
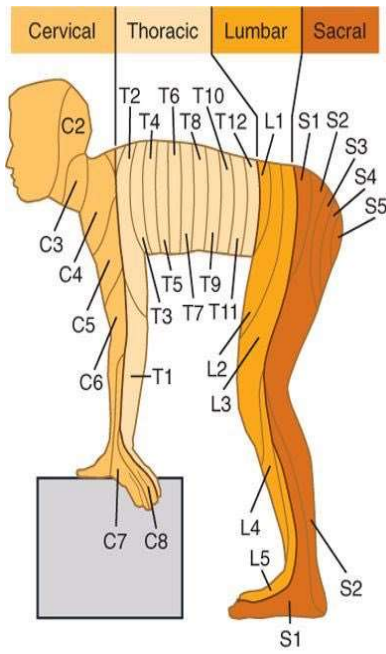
BLOOD VESSELS											
Arteries	<ul style="list-style-type: none">○ Their important properties have been explained in CVS Section.○ Here We Recap the imp features regarding General Anatomy and exam point of View.○ End arteries: having No precapillary Anastomosis, Present in Vital Organs; Retina > Spleen > Heart. True end artery in retina (Central Retinal artery). Functional end artery in Heart○ Network of Small vessels Supplying large vessels is VASA VASORUM (BCQ).○ Tubular structure with thick 3 layer of Muscles, Elastic Walls having internal Elastic Lamina & Adventitia around is MUSCULAR Artery (BCQ).○ Regarding Preferential thoroughfare Channels: (BCQ): follow This Sequence given.○ Have Smooth Muscles > Present on Precapillary Sphincters > Open on Demand										
Veins	<ul style="list-style-type: none">○ Medium Sized veins have valves (BCQ). Saphenous vein has 20 Valves (BCQ)○ Structure with Smooth Muscles longitudinally arranged in Adventitia = Large Sized Vein○ Veins Not having valve are : <table><tr><td>Openings of SVC & IVC</td><td>Very Small Veins < 2mm</td><td>Retinal Vein</td></tr><tr><td>Emissary veins, Dural Sinuses</td><td>Pulmonary & Umbilical veins</td><td>veins in Erectile tissue of Penis</td></tr><tr><td colspan="3">Cerebral vein, Portal vein, Hepatic vein, Renal vein, Ovarian and Uterine veins</td></tr></table>		Openings of SVC & IVC	Very Small Veins < 2mm	Retinal Vein	Emissary veins, Dural Sinuses	Pulmonary & Umbilical veins	veins in Erectile tissue of Penis	Cerebral vein, Portal vein, Hepatic vein, Renal vein, Ovarian and Uterine veins		
Openings of SVC & IVC	Very Small Veins < 2mm	Retinal Vein									
Emissary veins, Dural Sinuses	Pulmonary & Umbilical veins	veins in Erectile tissue of Penis									
Cerebral vein, Portal vein, Hepatic vein, Renal vein, Ovarian and Uterine veins											
Capillaries	<table><tr><th>Type</th><th>Examples</th></tr><tr><td>Continuous</td><td>Most common type. present in: Brain (Blood brain barrier) > Skin, Fat and Muscles</td></tr><tr><td>Fenestrated</td><td>They have pores. Present in Kidney, GIT & Endocrine glands (BCQ)</td></tr><tr><td>Sinusoidal</td><td>Aka Discontinuous type, most Leaky type e.g. in Liver Spleen and Bone Marrow</td></tr></table> <p>Capillaries have largest cross-sectional area for gases and nutrients exchange</p>		Type	Examples	Continuous	Most common type. present in: Brain (Blood brain barrier) > Skin, Fat and Muscles	Fenestrated	They have pores. Present in Kidney, GIT & Endocrine glands (BCQ)	Sinusoidal	Aka Discontinuous type, most Leaky type e.g. in Liver Spleen and Bone Marrow	
Type	Examples										
Continuous	Most common type. present in: Brain (Blood brain barrier) > Skin, Fat and Muscles										
Fenestrated	They have pores. Present in Kidney, GIT & Endocrine glands (BCQ)										
Sinusoidal	Aka Discontinuous type, most Leaky type e.g. in Liver Spleen and Bone Marrow										

NERVES	
Basic concepts	<ul style="list-style-type: none"> ○ Neuron is the basic Structural & functional unit of the nervous system. ○ Collection of neurons makes Nerves. ○ Neurons have A cell body (Soma), Axon/Dendrites, may be myelinated/Unmyelinated. ○ Nerve fibre: Axons (taking impulse away from the cell body) are generally referred to as nerve fibres e.g., A fibres, B fibres, C fibres etc. ○ Axon takes impulse away from Cell body while Dendrites send impulse toward cell body
Nerve vs Ganglion	<ul style="list-style-type: none"> ○ Nerve is bundle of fibres largely comprising of Axons. ○ Ganglion is a collection of Cell bodies of neurons outside CNS. ○ There are Cranial Nerves & Spinal Nerves in Body. ○ Ganglions can be sensory or autonomic. ○ Here we discuss SPINAL Nerves, Cranial Nerves will be described in HEAD & NECK region
Spinal nerves (31 pairs)	<ul style="list-style-type: none"> ○ Pairs: 8 Cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal pair ○ Formed by Union of Large Anterior & small Posterior Roots in intervertebral foramen. ○ They are mixed nerves (both Sensory & Motor) ○ Anterior Root has efferent motor fibres from T1-L2, autonomic fibres S2-S4, and, Unmyelinated pain fibres. ○ Posterior Root has Sensory afferent fibres whose cell bodies are in dorsal ganglia. ○ Preganglionic Sympathetic: Present in WHITE Rami. 14 white rami exist. ○ Postganglionic Sympathetic: present in ALL Spinal Nerves except C1. ○ NO SYNAPSES present in Dorsal Root ganglia (BCQ). ○ Anterior Ramus: Supply skin+ all Muscles of Limbs, also anterior neck, and trunk muscles ○ Posterior Ramus: Supply Intrinsic muscles of back & skin of back, also supplies splenius neck muscles and Erector Spinae muscles. ○ <u>Connective Tissues/Covering Around Nerve</u> <ol style="list-style-type: none"> Epineurium: Encloses Entire nerve Perineurium: Bundle of nerve fibres (Frequently asked BCQ) Endoneurium: encloses Individual nerve fibres, affected in Gullian Barre Syndrome ○ Sciatic Nerve is thickest nerve of body with 80% Connective tissue & 20 % nerve fibres. ○ Smaller Nerves have more neural tissue











DERMATOME VS MYOTOME				
DERMATOME	Area of Skin supplied by a single spinal nerve/dorsal Root (Derma means Skin)			
	C1 – No skin supply		T1 – Medial arm (Up + below)	L2 – anterior thigh, upper buttock
	C2 – Occiput, parotid skin		T2 – medial arm, axilla, thorax	L3 – knee (anterior, medial)
	C3 – Neck, supraclavicular		T4 – Nipple	L5 – medial leg + medial ankle
	C4 – shoulder, infraclavicular		T7 – Subcostal angle	L5 – lateral leg, medial sole, dorsum of foot
	C5 – lateral arm		T8 – Rib margin, abdomen	S1 – lateral ankle, lateral side of foot and dorsum of foot
	C6 – thumb, lateral forearm		T12 – upper buttock, lower abdomen	S2 – posterior leg and thigh
	C7 – middle finger, elbow		L1 – suprapubic, inguinal area, penis, and labial area	S3 – sitting area of buttock, posterior scrotum, anal region
	C8 – little finger, medial forearm			S4 – Peri- anal region
MYOTOME	Group of Muscles innervated by Single Spinal nerve/ anterior root.			
	Elbow	Flexion: C5 C6 Extension: C6, C7	Knee	Flexion: L5, S1 Extension: L3, L4
	Forearm	Supination: C6 Pronation: C6, C7	Ankle	Dorsiflexion: L4, L5 Plantarflexion: S1, S2
	Hand	Intrinsic muscles C8 – T1	Foot	Inversion: L4 Eversion: L5, S1
Tendon reflexes	Biceps jerk	C5, C6 (C6*)	Knee jerk	L3 > L4
	Triceps jerk	C7, C8 (C7*)	Ankle jerk	S1, S2 (S1*)

KEY FACTS

✚	Thumb, Deltoid, Biceps affected due to Lesion of C6
✚	All short muscles of hand damaged due to damage to C8-T1 > T1 lesion
✚	Sensory Supply from Neck to Supraclavicular is C2-C3 . For infraclavicular C3-C4
✚	So C3 for above Clavicle, C4 For below Clavicle (BCQ)
✚	A student having neck pain while studying, at which level transactions need to be done = At C3 Level .
✚	High collar shirt / high neck – C3, while lower collar shirt – C4.



COMMUNITY MEDICINE, BIOSTATS & BEHAVIORAL SCIENCES

Levels Of Prevention	Modes Of Intervention	Examples
Primordial Aims to Reduce the emergence of risk factors.	 Health promotion  Health education	 Avoiding risk factors for: cancers or IHD.
Primary (Prevention) Prevents onset of disease by Managing risk factors	 Specific Protection  Reduces the Incidence of disease	 Vit A & D prophylaxis Vaccination i.e., EPI
Secondary (Screening) Asymptomatic disease stage	 Early Diagnosis & prompt intervention  Reduces the Prevalence	 Screening tests e.g., Pap Smear Mammography etc.
Tertiary (Treatment) Clinical onset of disease	 Disability Limitation & Rehabilitation	Vocational / educational rehab etc.

EPIDEMIOLOGICAL STUDY DESIGNS

Descriptive Studies		Analytical Studies	
<ul style="list-style-type: none"> ○ If comparing populations: a. Ecological design (correlation) 	<ul style="list-style-type: none"> ○ If comparing individuals: a. Case report b. Case series c. Cross sectional studies 	<ul style="list-style-type: none"> ○ Observational a. Case control b. Cohort studies Cohort study types: <ul style="list-style-type: none"> ❖ Retrospective ❖ Prospective prospective is the better study design 	<ul style="list-style-type: none"> ○ Experimental a. Randomized controlled trials (RCTs) E.g., testing drugs. b. Field trials (High risk members of population) c. Community trial (evaluate the lifestyle interventions)

SUMMARY + IMPORTANT FACTS

- Cohort study proceeds from Cause to effect while Case Control goes from Effect to Cause.
- Cohort study Tests whether disease occurred more frequently in those Exposed to Risk factors or not exposed to risk factors i.e., group with risk factors & grp without Risk factors.
- CASE Control tests whether suspected CAUSE occurs more frequently in those with Disease or those without disease i.e., study of affected/non affected. It Determines Odds ratio.
- Cohort study can be Retrospective (Past) or Prospective (Looking Forward; that is better)
- Case Control is applied on RARE Diseases, involves few individuals and is relatively inexpensive.
- The natural history of disease is best established by Cohort studies.
- ODDS ratio is calculated from Case control whereas Relative risk and Attributable risk from Cohort.
- Cross sectional studies are like Survey that helps to find Prevalence / Frequency of disease.
- Cross sectional study Helps to find association of disease/ relation of disease with risk factors.
- So, cohort & case controls involve groups whereas no groups in cross sectional studies.
- Randomized Control Trials are used in assessing Treatment protocols e.g., pharmacological, or operative/ surgical.
- Cohorts study involves Long follow up; therefore, are Susceptible to Bias
- Attrition bias is linked to follow up + prognosis. Berkson's Bias is related to different exposure.
- Randomization/matching eliminates Confounding bias.
- Incidence rate considers only new cases of a disease.
- Prevalence rate considers all (new + old) cases of a disease.
- Incidence rate considers population at risk as a denominator.
- Prevalence rate considers total population as a denominator.
- Incidence & period prevalence rates require follow up studies.
- Point prevalence rate requires cross- sectional study.
- Experimental Study involves single / double / triple blinding.
- Single blinding: study subjects don't know to Which group they belong.

- Double blinding: Caregivers also don't know to Which group study subjects belong.
- Triple blinding: data collectors also don't know. Allocation status
- Advantage of Blinding is that it Avoids observation bias.
- **Attack Rate**: Proportion of people exposed who become ill. (People becoming ill/ total exposed).
- **Secondary Attack Rate**: No. of exposed people developing disease within Incubation period \times 100 divided by Total persons exposed to primary case.
- **Index case** (patient) is defined as the first reported case of the disease that is diagnosed by clinician or epidemiologist.
- **Primary case** is a person who gets the disease from exposure and first case in a population.

Relative Risk (RR)	Odds ratio (OR)
$a / a + b$	a/b OR = ad / bc
$c / c + d$	c/d

Exposure Status		Event Occurred	
		YES	NO
Exposed		a	b
Not Exposed		c	d
Interpretation Of Relative Risk & Odds Ratio			
<ul style="list-style-type: none">○ RR = 1: No association between exposure & disease○ RR > 1 : Exposure associated with inc occurrence of disease.○ RR < 1 : exposure associated with Dec disease occurrence		<ul style="list-style-type: none">○ OR = 1 : Odds of exposure are equal in Cases and control.○ OR > 1: Odds of exposure are More in cases than control.○ OR < 1: Odds of exposure are greater in Controls	
Measures of Central Tendency (Mean, Median And Mode)	Mean	<ul style="list-style-type: none">✚ The mean is the average or normal. Add up all the values to find a total. Divide the total by the number of values you added together. $2 + 2 + 3 + 5 + 5 + 7 + 8 = 32 \rightarrow 32 / 7 = 4.57$✚ Mean is the best measure of central tendency in normal distribution curve.✚ Mean is most affected by Extreme values (most robustness) while Mode is the Least robust	
	Median	<ul style="list-style-type: none">✚ The median is the middle value. Put all the values into order, The median is the middle value. .✚ If there are two values in the middle, find the mean of these two.	
	Mode	<ul style="list-style-type: none">✚ The mode is the most frequent value.✚ Count how many of each value appears. The mode is the value that appears the most.✚ You can have more than one mode in a data.	

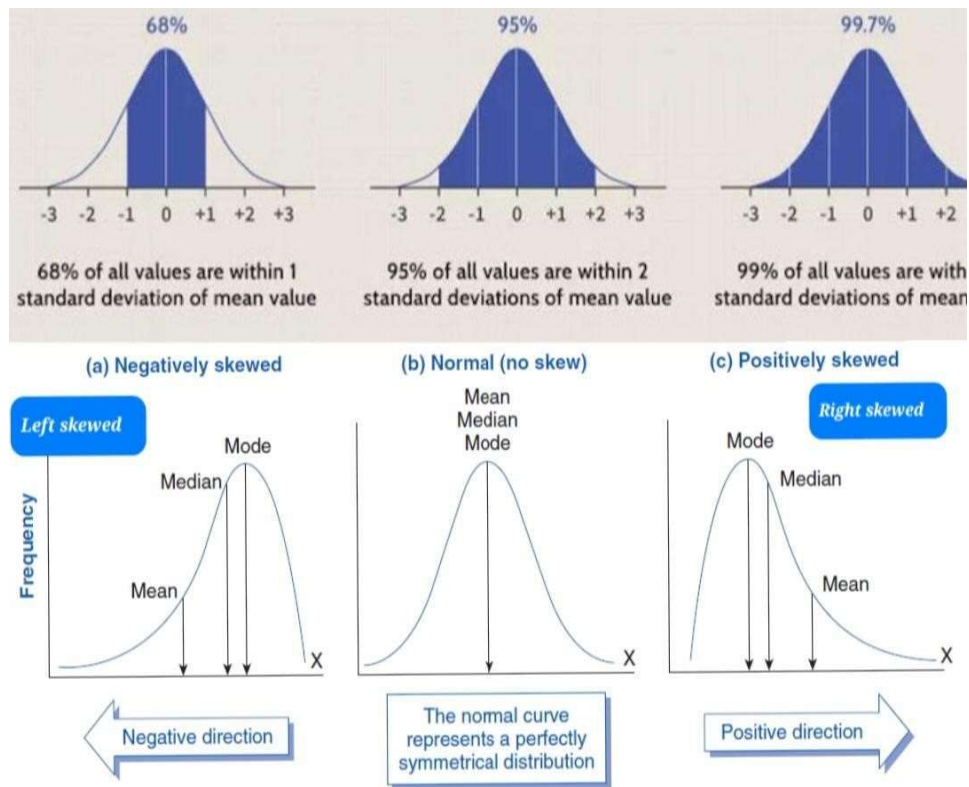
Measures Of Dispersion	<ul style="list-style-type: none"> Range, Interquartile Range, Standard Deviation, and Variance. Variance is Square of standard deviation (SD) and measure of Variability. Standard deviation implies how much Variability exists in values around Mean. Probability of difference between two means is a test of Significance. Standard deviation is Square Root of Variance . Standard Error is an estimate of how much variability exist around true population mean. Confidence Interval: depends on Mean & Standard Error. Confidence Limit: depends on T value & Standard Error (Note T at end of Limit).
-------------------------------	--

<ul style="list-style-type: none"> ○ Sample is a part of Population and group of people with a specific feature are represented by Frequency or Occurrence.
<ul style="list-style-type: none"> ○ T test is used for checking difference between mean of 2 groups. ○ ANOVA Test for Mean of 3 or more groups.
<ul style="list-style-type: none"> ○ Chi Square Test for Categorical data & comparing the difference of Proportions / Percentages (not Mean values). ○ When the sample is small, we use Fisher's exact test instead of Chi square for percentages.
<ul style="list-style-type: none"> ○ The 2 × 2 table as given below is applied on the Chi square test.
<ul style="list-style-type: none"> ○ Meta-analysis combines data from different studies. ○ Regression analysis is used to compare the relationship of variables e.g., temperature changes with general anaesthesia over time.
<ul style="list-style-type: none"> ○ As sample size inc, mean increases, Standard deviation + SEM are Decreased whereas Confidence interval narrows

CONTINGENCY TABLE OR 2X2 TABLE			
	Disease	No Disease	Total
Exposed	A	B	A + B
Non-Exposed	C	D	C + D
Total	A + C	B + D	A + B + C + D

STANDARD DISTRIBUTION CURVE

- Also known as Gaussian curve
- bell shaped curve , mean = 0, Standard deviation = 1, mean = median = mode
- Total Area of Standard Normal distribution curve is 1. Mean = 0, SD or Variance = 1
- 1 SD → 68%, 2 SD → 95%, 3 SD → 99.7%
- Normal distribution curve is Bilaterally Symmetrical
- Positive Skewed/ Right skewed means that → Mean > Median > Mode. Longer tail on right side.
- - Ve skewed/ left skewed → mode > median > mean.
- For accurate confidence interval → **Increase the Sample Size**
- At 90 % Confidence Z value is **1.64**
- for 95% Confidence level (**frequently 95% CI is used**) -- Z value is **1.96**
- For 98% -- Z is **2.33**.
- **For 99% confidence -- Z is 2.58**
- When confidence interval is **95%**, then margin of error is 5 %
- Confidence interval = 1 - alpha.
- As the sample size increase → the **CI narrows**.



SCREENING & SAMPLING

True Positive (TP)	True Negative (TN)	False Positive (FP)	False Negative (FN)
<ul style="list-style-type: none"> test is +ve and pt has the disease as well 	<ul style="list-style-type: none"> test is -ve and pt has not disease as well 	<ul style="list-style-type: none"> Test is +ve in the absence of disease 	<ul style="list-style-type: none"> Test is -ve in the presence of disease
Sensitivity (TP/TP + FN)	Specificity (TN/TN+FP)	Positive Predictive value PPV = (TP/TP+FP)	Negative Predictive Value (TN/TN+FN)
<ul style="list-style-type: none"> ability of a test to correctly identify those who have the disease. i.e., (True + ve rate) Sensitivity rules IN disease sensitive tests are Screening tests 	<ul style="list-style-type: none"> Ability of a test to identify those who are without disease i.e., (True – ve rate) Specificity rules OUT disease. Specific tests are Confirmatory tests 	<ul style="list-style-type: none"> percentage chance that a pt with +ve test actually has the disease 	<ul style="list-style-type: none"> Percentage chance that a pt with -ve test is actually disease free.
<p>PPV & NPV Vary Depending on Disease Prevalence.</p> <p>But Prevalence Has No Effect on Sensitivity / Specificity.</p> <p>Prevalence = $\frac{TP + FN}{TP + TN + FP + FN}$</p> <p>Lowering Cut Off Value of Test : \uparrow FP Rate Leads to \uparrow Sensitivity + NPV But \downarrow Specificity + PPV.</p> <p>Raising Cut Off Value of Test : \uparrow FN Rate Leads to \uparrow Specificity + PPV But \downarrow Sensitivity + NPV .</p> <p>PPV = positive predictive value; NPV = negative predictive value.</p>			
Test Result	Disease Present	Disease Absent	Sensitivity = $A/A+C$ Specificity = $D/B+D$
Test Positive	True Positive (A)	False Positive (B)	
Test Negative	False Negative (C)	True Negative (D)	

Precision (Reliability or Consistency)	Accuracy (Validity)
<ul style="list-style-type: none"> ○ Test repeatedly gives same result or value. ○ Increased precision has following effects: <ul style="list-style-type: none"> a. Increased reliability. b. Decreased random error. c. Decreased standard deviation. 	<ul style="list-style-type: none"> ○ How well the given measurement represents the truth ○ Increase in accuracy has these effects: <ul style="list-style-type: none"> a. Decrease in Bias b. Increased validity

TYPES OF DATA

1. Quantitative

- Data that can be measured with numbers such as duration/speed.
- It may be discrete or continuous.
- I. **Discrete data** : whole number that can't be broken down such as number of items.
- II. **Continuous data** : numbers that can be broken down further such as height/weight.
It may be of 2 types :
 - a. **Interval** : numbers with known difference between values such as time.
 - b. **Ratio scale**: numbers that have measurable intervals where difference can be calculated such as height/weight.

2. Qualitative

Non numerical data that is categorical such as Yes/No response or eye color. It is of 2 types:

- i. **Nominal** : data used for naming variables such as hair color.
- ii. **Ordinal** : data used to describe order of values such as 1 = happy, 2 = neutral, 3 = Unhappy.

Key Facts

- To represent qualitative data we use Bar Chart, Pie Chart and Frequency Table.
- Pie Chart Uses Percentages % To Represent Data E.G 72% 22% 6% Etc.
- Test applied for categorical data is the CHI square test.
- To represent quantitative data, we use Histogram.
- Tests applied for quantitative data are T-Test, ANOVA, Correlation, Regression Analysis.
- P-value is Significance when less than 0.05.
- Correlation Is Represented By R, Value Is +1, And -1. Value Of Zero Is No Correlation
- Value Of +1 And Greater Is Positive Correlation. Value Of -1 Is Negative Correlation

Random sample	Defined as where each member of population has an equal chance of selection.	
Types of sampling	There are two types of sampling : Probability sampling Or Non-probability sampling.	
	Probability Sampling Types	Non- Probability Sampling
	<ul style="list-style-type: none"> ❖ Random Simple sampling: everyone has Equal chance of selection. ❖ Systemic Random sampling ❖ Stratified Random sampling: where People/data/sample is divided into groups & randomly selected ❖ Cluster sampling. ❖ Multistage sampling 	<ul style="list-style-type: none"> ❖ Purposive sampling ❖ Convenience sampling ❖ Quota sampling ❖ Snowball sampling

STATISTICAL HYPOTHESIS TESTING	
Null Hypothesis (H0)	Hypothesis Of No Difference/ H0 <ul style="list-style-type: none"> Null hypothesis claims that there is no relationship (difference) between two groups being Compared and denoted by Ho. if we want to know the complication rate of Abdominal and vaginal hysterectomy. Null hypothesis claims that there is no difference between the two surgical procedures with respect to postoperative complications
Alternate Hypothesis (H1)	<ul style="list-style-type: none"> It states that the different sets of data belonging to different Populations are statistically significant and are not due to chance. In other words; Compare the calculated value of test statistics with critical values of Z / t / X2 and then Accept or reject the null hypothesis.
Testing Errors	Type 1 Error or Alpha Error / False Positive Error : <ul style="list-style-type: none"> The incorrect rejection of a true Null hypothesis/ H0 is called type 1 error. We wrongly reject the H0. Example: A test that shows that a patient to have a disease when in fact the patient does not have the disease Type 2 Error or Beta Error / False Negative Error <ul style="list-style-type: none"> It is the failure to reject a false null hypothesis i.e., accepting a False Null Hypothesis. Example: Blood test failing to detect the disease it was designed to detect in a patient who really has the disease.
P VALUE	<ul style="list-style-type: none"> The probability of committing type 1 error rejecting H0 when it was true) is Known as P - value. Researchers throughout the world agree that a chance of error up to a maximum of 5% (0.05 in terms of probability) is reasonable in making decisions about Ho. If P-value is less than 5% or 0.05 then H0 is rejected

MEDICAL ETHICS

(Branch of **Behavioral Sciences**. It has 4 pillars / Principles)

Principle	Explanation
1. Autonomy	To Provide Conditions for Patients for Autonomous/ Self-Choice by Honouring their Preferences e.g., Informed Consent
2. Beneficence	To Act in The Best Interest of Patient
3. Non-maleficence	Do Not Harm. If Benefits Outweigh Risks, Patient Can Make Informed Decision to Proceed
4. Justice	To Treat Fairly on The Principles of Equity Rather Than Equality.

Informed Consent	<ul style="list-style-type: none"> A process that explains the proposed treatments option with their benefits & Risks and alternative options available, including No treatment It requires disclosure of information, Understanding, Capacity to make own decision and Voluntariness. Pt must be informed of their right to revoke written consent at any time even Orally Exceptions include : <ul style="list-style-type: none"> Emergency situations: implied consent may apply. Therapeutic privilege: withholding info when disclosure will harm pt. Legally incompetent: Pt lacks decision making capacity (obtain it from legal surrogate) Waiver: Pt relinquishes the right of informed consent
Consent for Minors (< 18 years old)	<ul style="list-style-type: none"> Parental consent is obtained unless until the pt. is married / independent or in Military. Exceptions where even parental consent is not required include: Drugs intoxication, STDs ,contraception, and emergency / Trauma.

Confidentiality

- Hippocratic Oath stresses upon the importance of confidentiality.
- It respects Autonomy & privacy of patient.
- It must not be breached at any cost whereas few exceptions exist .
- Patients can waive the right to confidentiality. In emergent conditions, disclosing info to family and friends must be guided by professional judgement of the patient's best interest.
- Exceptions where you can breach Confidentiality:
 - ✚ Pt with Suicidal / Homicidal ideas
 - ✚ Epilepsy and other impaired automobile drivers
 - ✚ Abuse i.e., child / adult / prisoners
 - ✚ STDs e.g., HIV / hepatitis
 - ✚ Food poisoning or dangerous communicable diseases like TB / Ebola etc.

IMPORTANT POINTS TO REMEMBER & ETHICAL SCENARIOS

Informational Care Session: aims at removing all myths or misconceptions about disease - providing correct info.

While Breaking Bad News: it must be in a formal manner in a physician's office / other isolated private place. Telling the patient about the disease in one-to-one session. Obtain the patient's permission to disclose and what necessary info is required about disease. If the patient feels ready, then discuss treatment options and goals of care.

Use Of Interpreters either for spoken or sign language; interpreter must be next to or slightly behind the physician.

While Gender & Sexuality Inclusive History Taking: use gender neutral terms e.g., refer to a patient partner rather than assuming a spouse's gender. As the pt. sex assigned at birth and gender identity may differ.

if some family member asks for info about pt. disease prognosis: Avoid discussing issues with relatives without patient's permission .

If Patient Is Suicidal: Suggest remaining in hospital /pt is involuntarily hospitalized.

If Parents of Child Refuse Vaccination: explain risks and benefits but don't administer without parents' consent

A Patient Who Is Required to Be Put on Ventilator: explain the need and procedure to pt and relatives

if family of a patient/ member of pt family asks you to not disclose results of a test to patient if prognosis is poor as patient can't handle it: Explain that if the patient wants to know about it then it will not be withheld. However, if you feel that disclosing info can seriously harm the pt, you can withhold info.

If A Child Loses Sister and Feels Responsible for That: reassure that he is not responsible

In Case of Intimate Partner's Violence: ask pt to make an emergency plan and educate on intimate partner's violence resources. Don't pressurize the pt to leave a partner or report to authorities etc.

when an invasive test is performed on wrong pt: physician must inform that pt that mistake has been made

if a patient complains about staff behaviour: Apologize to the patient and tell them that you will talk to the staff regarding it.

FREQUENTLY ASKED BCQs

- In Behavioral Sciences the Bio-Psycho-Social (BPS) model of health care is best described as = **Use of social and psychological factors alongside the biological aspects of the illness**
- 12 years old male did not need to be told that he had failed his exams. On returning home he could guess by the looks on his father's face and his posture, what his result was. This is an example of = **Non-verbal Communication**
- Regarding counselling, the best statement is = **It is a technique to help people help themselves by increasing self-understanding.**
- A common misconception about counselling is that it = **Involves giving direct advice to clients.**
- Conflict resolution involves: **Dealing with difficult issues Sooner rather than later.**
- Which of the following ethical issues form the foremost part of Hippocratic oath: **Confidentiality.**

- A female patient comes to the doctor's clinic wearing revealing clothes. She comes up very close to the doctor and starts asking him personal questions in a seductive tone. What would be the appropriate response by the doctor = **Call in a nurse.**
- Patients are most likely to comply with the medical advice for which of the following reasons = **The doctor has taken time to provide Informational Care to the patient.**
- A competent 30-year-old lady who is 38 weeks pregnant refuses to have a caesarean delivery even though without surgery, the fetus could die. Both her surgeon and psychiatrist have failed to convince her to have the surgery. The most appropriate action for her surgeon to take currently is to = **Deliver the child vaginally**
- "Fight or flight response" is the responsibility of the following System = **Sympathetic division of ANS**
- A final year medical student and while reading through the medical documents of a psychiatric patient feels puzzled by the term "alexithymia". Which of the following best describes this state = **Difficulty talking about and expressing emotions**
- Behavioral modification involves = **Application of learning principles to change behavior.**
- Negative reinforcement means: **To extinguish a behavior.**
- classical conditioning technique used to eliminate phobias: **Systematic desensitization.**
- Little Mobeen has recurrent allergies and must receive injections to counteract them. He became fearful and cried whenever he got his injections but now just the sight of a nurse makes him fearful and tearful. What is the conditioned stimulus in this example = **Injection**
- To teach your dog to roll over on command, which of the following techniques would you use = **Shaping**
- In classical conditioning what happens to a neutral stimulus after it is associated with the unconditioned stimulus = **it becomes a conditioned stimulus**
- A father scolds his son when he hits his little sister. The son stops hitting the sister. This change in the child's behavior is a result of = **punishment**
- After a serious car accident, Pt cannot remember any new information. This deficit is an example of = **Anterograde amnesia**
- Disease and hospitalization are a source of major stress to the patient. One of the urgent concerns of the patient when he meets a doctor is: = **What is wrong with me?**
- The basic skill of active listening which is the cornerstone of Effective communication is = **Understand both what the patient and the physician are saying and the undercurrents of unspoken feelings between the two.**
- Reaction of the patient toward the psychiatrist may be affected by = **Stigma associated with a psychiatrist.**
- The best method to facilitate the development of doctor-patient rapport is = **Using patients own words / Recapitalization**
- A TV Compeer becomes terrified of speaking in public. He cancels his speaking engagements for fear of forgetting embarrassment. He seeks treatment and is taught first to relax completely, and then, while relaxed, imagine going to a lunch, then sitting on the platform, then rising to introduce the guests, and so forth. Best statement that can be made about this situation is = This overall approach is called Systematic Desensitization.
- The best example of verbal communication skill is **Competence in presentations** > Fluent speech.
- Regarding roles, in one role one is a student, in another; a father, a teacher, a scientist, a bread earner and a sportsman = **This is explained by: Dynamism**
- 25-year-old doctor brings his 50-year-old father who has suddenly met a traffic accident and suffered serious injuries, to the casualty department of the hospital. Incidentally the surgeon arrives late to examine the patient. By the time he examined the patient, he had already passed into a state of unconsciousness with failing breathing. All resuscitative measures failed, and the patient died. At that time the son felt the shock (shock and numbness) but immediately adopted a posture that surprised everybody. He insisted that his father should be taken to intensive care and put on a ventilator, and that he was in fact "not really dead". The phenomenon which best describes the clinical scenario is = **DENIAL**
- The Defense mechanisms = **Help individuals cope with their internal and external states of anxiety and distress.**
- Patient experiences stress of hospitalization due to: **Structure and functioning of hospitals.**
- Which one of the following is best example of psychosocial stress: **Economic viability** > Noise 31. People with Type A personality is more vulnerable to **Increased incidence of heart disease.**
- Common characteristics of Type B person are: **Easy going** > **Non-competitive.**
- Culture: **Is the outcome of the man-made part of our environment.**
- Social structures are **Systems of socioeconomic stratification / placing people in social strata.**

- Mutual prayer such as “Only Allah granted health” (Allah hi Sehat Deta Hai) is an example of = **BELIEF**
- The sick role (patient role) involves: **Being excused from various obligations.**
- Bilal is an 8-year-old boy who still wets his bed almost every night. He is ashamed of this and is ridiculed by his cousins. His parents are worried and take him to a doctor who refers him to a psychiatrist. He was given a buzzer which would sound the moment Bilal passed urine in bed at night, thus waking him up. The idea was to associate the stimuli from a full bladder and the urge to urinate with waking up. If Bilal woke up in time, he could go to the bathroom before he could wet his bed. This treatment is based on the principles of = **Classical conditioning**
- Modelling: **Is an observational form of learning.**
- Clairvoyance is = **The ability to perceive events or gain information in ways that appear unaffected by distance or normal physical barriers**
- Emotionally intelligent people can Accurately perceive emotions.
- The concept of justice in ethics is: **That the health resources must be distributed according to principles of equity.**
- Confidentiality can be breached: **When a patient authorizes to do so.**
- Regarding relationship with the pharmaceutical industry = **There should be mutual pooling of resources to promote welfare of the health institutions.**
- An adult patient in a medical ward may start to insist on being examined by one particular doctor, feels that the same doctor Comes to his bed first and wants to spend a longer time in the Company of the same doctor. The doctor, on account of his physical appearance, mannerism, or personality qualities, reminds the patient of his or her father. This can be explained by the phenomenon of = **TRANSFERENCE**
- **Medical Ethics Is the study of moral aspects of a doctor’s professional life.**
- **Active Listening** Is important in effective Communication.
- Lack of Communication or hurried approach creates.: **Mistrust**
- Doctor -Patient rapport is maintained by **Polite Behavior at bedside.**
- A Pt crying to talk about relative death what should be your response: **Take your time.**
- A student continuously failing in exams is doing anger to parents is which response: **DISPLACEMENT.**
- **Extensive Expertness prevents complications. Doctor must not cross his competency level.**
- **Idiosyncrasy is related to psychological components.**
- ARTHQUAKE / FLOOD are examples of **Situational Crisis**
- Disease Monitoring is done by **Predictive Value**
- ALPHA value 0.001 in stats represents: **chance of rejecting the null hypothesis correctly in 1/1000.**
- **KAPLAN – MEIER curve indicates: SURVIVAL Of patient.**
- Behavioral changes are produced by: **Peer seeder.**
- Yellow fever in non-Endemic area is called **Sporadic.**
- **Test which completely excludes non affected is SPECIFIC test.**
- **RANDOM SAMPLING involves equal chance of each person being selected.**
- Equity is closely **related to Justice** in biomedical ethics.
- Females have Mean RBS 200 ± 50 ; whereas males have means RBS 205 ± 10 the results revealed that
- Females have Higher standard deviation (50) and Lower Mean (200 as compared to 205 in males) in their group.
- **Maternal Mortality rate inc 100 times in Pak**
- **Maternal Mortality Rate = No. of Maternal deaths in 1 year $\times 100000$ / Average women in reproductive age in that same 1 year**
- **Maternal Mortality Ratio= No of Maternal deaths in 1 year $\times 100000$ / no. of Live Births in same 1 year**
- **CASE fatality rate = Number of deaths from disease/ total cases. For Rabies CFR Is 100%**
- **Perinatal mortality includes deaths from 28wks of gestation to 07th day of birth, includes both Liver births + Stillbirth in denominator.**
- In Two tailed test: **area of distribution is two sided. Used in null hypothesis.**
- P value is significant if: **Less than 0.05**
- **Variance = Standard deviation + Mean**

PHARMACOLOGY

Pharmacokinetics	<ul style="list-style-type: none"> What the Body does to the drug or the effect of body on drug. It includes Absorption, distribution, metabolism, and excretion (ADME). Example : Lithium & Thiazide interaction (inc toxicity of Lithium). Increased Methotrexate toxicity with Aspirin. It can be applied on Rational drug Use /design. Retepase , Alteplase are examples of rational drug designs. 						
Pharmacodynamics	<ul style="list-style-type: none"> What the drug does to the body/ effect of drug on body. It includes Mech of action drugs, their biochemical /physiological functions. Example : Morphine & Naloxone drug interaction (to reverse the morphine action). Blockade of Ach receptors by Atropine. Prevention of Nitro-glycerine induced tachycardia by Propranolol. 						
Enzyme kinetics	<p>Michaelis-Menten kinetics</p> <ul style="list-style-type: none"> Km is inversely to enzyme affinity for substrate. Vmax is directly proportional to enzyme concentration. Hyperbolic curve : Most enzymatic reactions Sigmoidal curve : indicated co-operative binding e.g., Hemoglobin. Lineweaver Burk Plot The higher the Km – the lower the affinity. Competitive inhibitors increase Km. 						
PHARMACOKINETICS INTERACTIONS (ADME)							
Absorption (A) (Drugs that is best absorbed is highly lipophilic yet soluble in aqueous solution)	<p>During absorption may occur in the:</p> <ol style="list-style-type: none"> Lumen (direct interaction) : Tetracycline or iron given with antacid cause formation of insoluble compounds Cholestyramine given with thyroxine digoxin also form insoluble complexes. Sucralfate + Phenytoin can cause the formation of insoluble compounds. Due to alteration in the gut flora: Antimicrobials (which inhibit the bacterial synthesis) given with oral anti-coagulants, may cause bleeding. Motility changes: The Anti-Muscarinic drug given with morphine decrease its absorption. Purgative given with steroids or digoxin decrease the time for absorption. Absorptive through other than oral route: Hyaluronidase with S/C drug help in spreading. Vasoconstrictors with S/C drugs, prolong local anaesthetic effect. 						
Volume of Distribution (Vd)	<ul style="list-style-type: none"> Relationship between amount of drug in the body to its concentration in plasma. Vd = amount of drug in the body/plasma drug concentration. Vd is not affected by gender. Depends upon plasma protein binding and binding to other tissues in body There are 3 types through which interaction occurs: During Protein binding: Sodium valproate given along with Phenytoin, displaces Phenytoin sodium from its protein binding and inhibits its metabolism. Albumin binds Acidic drugs (A-A), while alpha glycoprotein binds basic drugs. Direct in blood: Protamine given with heparin, antagonize it. Deferoxamine given with iron, antagonize it. Dimercaprol antagonizes arsenic. During tissue binding Quinidine displaces digoxin leading to inc toxicity. Naloxone given to interact with morphine receptors. Different CNS depressant, augment each other dressing effects. Verapamil given with beta-blocker, causes bradycardia or heart block. Thiazide diuretic given with lithium, cause lithium toxicity. Haemodialysis is most effective for drugs with low Vd. 8 Litre Vd → there is more protein binding and less drug available in the blood. <table border="1" style="width: 100%; margin-top: 10px;"> <tr> <td>Low Vd</td><td>Drug is distributed in Intravascular compartment e.g., Plasma.</td></tr> <tr> <td>Medium Vd</td><td>Drugs is distributed in Extracellular fluid ECF.</td></tr> <tr> <td>High Vd</td><td>All tissues distribution including fat</td></tr> </table>	Low Vd	Drug is distributed in Intravascular compartment e.g., Plasma.	Medium Vd	Drugs is distributed in Extracellular fluid ECF.	High Vd	All tissues distribution including fat
Low Vd	Drug is distributed in Intravascular compartment e.g., Plasma.						
Medium Vd	Drugs is distributed in Extracellular fluid ECF.						
High Vd	All tissues distribution including fat						
Biotransformation or Drug Metabolism	<p>The series of changes a drug undergoes in body – how it is altered or terminated.</p> <p>Major site of drug metabolism is Liver, others are kidney, lungs, GIT, or skin.</p>						

	<p>Two phases as given.</p> <table border="1"> <tr> <td>Phase I reactions</td><td> <ul style="list-style-type: none"> They include Oxidation, reduction, hydrolysis, and hydroxylation dependant on CYP 450. This makes the drug slightly polar (water soluble) active on inactive. Hydroxylation is the main mechanism. Geriatric patients (elderly) lose phase I reactions first. </td></tr> <tr> <td>Phase II reactions</td><td> <ul style="list-style-type: none"> They include Glucuronidation, acetylation, methylation, and sulfation. As a result, very polar metabolite is formed except by acetylation. Elderly patients have more active Phase 2 reactions. Patients who are slow acetylators e.g Asians have increased side effect from certain drugs due to low rate of metabolism (isoniazid). </td></tr> </table>	Phase I reactions	<ul style="list-style-type: none"> They include Oxidation, reduction, hydrolysis, and hydroxylation dependant on CYP 450. This makes the drug slightly polar (water soluble) active on inactive. Hydroxylation is the main mechanism. Geriatric patients (elderly) lose phase I reactions first. 	Phase II reactions	<ul style="list-style-type: none"> They include Glucuronidation, acetylation, methylation, and sulfation. As a result, very polar metabolite is formed except by acetylation. Elderly patients have more active Phase 2 reactions. Patients who are slow acetylators e.g Asians have increased side effect from certain drugs due to low rate of metabolism (isoniazid).
Phase I reactions	<ul style="list-style-type: none"> They include Oxidation, reduction, hydrolysis, and hydroxylation dependant on CYP 450. This makes the drug slightly polar (water soluble) active on inactive. Hydroxylation is the main mechanism. Geriatric patients (elderly) lose phase I reactions first. 				
Phase II reactions	<ul style="list-style-type: none"> They include Glucuronidation, acetylation, methylation, and sulfation. As a result, very polar metabolite is formed except by acetylation. Elderly patients have more active Phase 2 reactions. Patients who are slow acetylators e.g Asians have increased side effect from certain drugs due to low rate of metabolism (isoniazid). 				
Enzyme inducers	<ul style="list-style-type: none"> Cytochrome P 450 Inducers decrease the concentration of other drugs. Examples: Barbiturates, phenobarbital phenytoin, carbamazepine, Rifampin, sulfonylureas, Alcohol (chronic), Griseofulvin, St. John's wort, smoking Phenobarbital (enzyme inducer) increases the metabolism of warfarin necessitating the increased dosage of warfarin. 				
Enzyme inhibitors	<ul style="list-style-type: none"> Cytochrome P 450 Inhibitors increase the concentration of other drugs i.e increased toxicity). Valproic acid, isoniazid, cimetidine, erythromycin, grapefruit juice, alcohol (acute) ketoconazole, fluconazole, omeprazole, Quinidine, chloramphenicol Increased toxicity of warfarin with cimetidine is an example of enzyme inhibition 				
Elimination	<p><u>Zero Order Elimination</u></p> <ul style="list-style-type: none"> Constant amount of drug eliminated per unit time and follow non-linear kinetics. Rate of Elimination dependant on Plasma drug concentration. Concentration decreases as 100mg → 80mg → 60mg → 40mg → 20mg. Clearance is more at low concentrations. Half-life is less at low concentration and more at higher concentrations (No fixed half-life). E.g. Alcohol, Phenytoin, Warfarin, Theophylline. <p><u>First Order Elimination</u></p> <ul style="list-style-type: none"> Constant fraction of drug eliminated per unit time and follow Linear kinetics. Concentration decreases as 100mg → 50mg → 25mg → 12.5mg. Rate of Elimination is Independent of plasma drug conc. Clearance and half-life remain constant. Flow dependant elimination. Most drugs follow 1st order elimination e.g paracetamol, naproxen etc. 				
Bioavailability (F)	<ul style="list-style-type: none"> Fraction of the drug that reaches systemic circulation unchanged. For IV drugs F = 100. Measures rate and extent of therapeutically active drug. 				
Clearance	<ul style="list-style-type: none"> The rate at which drug is being removed from the body. CL = rate of drug elimination/plasma drug concentration. 				
Half Life T_½	<ul style="list-style-type: none"> The time required for the drug to decompose to one half its original concentration. $T_{½} = 0.7 \times V_d / Cl$ Shelf-life t -90% is the time required for the drug to lose 10% of its original concentration. Or it's the time required for the drug to degrade to 90% of its original concentration. 				
PHARMACODYNAMICS					
Dose response curve (DRC)	<ul style="list-style-type: none"> Steep slope: a moderate increase in dose markedly increases the response (dose not individualizes). Flat DRC: little increase in response occurs in a wide range of doses – standard dose can be given to most patients. 				
Efficacy (E max)	<ul style="list-style-type: none"> The Max effect a drug can produce regardless of dose. A Measure of drug activity. 				
Potency (EC 50 or ED 50)	<ul style="list-style-type: none"> Dose or amount of drug required to produce a desired effect. A measure of drug affinity. 				
Median effective dose (ED 50)	<ul style="list-style-type: none"> The dose at which 50% of individuals exhibit the specified quantal effect. Quantal dose-response graphs can be characterised by the median effective dose (ED50). 				
Median toxic dose	<ul style="list-style-type: none"> TD 50 = The dose required to produce a defined toxic effect in 50% of subjects. 				
Median lethal dose	<ul style="list-style-type: none"> The dose required to kill 50 % of subjects. 				

Therapeutic index	<ul style="list-style-type: none"> The ratio of the TD 50 /ED50 , a parameter which reflects the selectivity of a drug to elicit a desired effect rather than toxicity. Lithium has narrow TI.
Therapeutic window	<ul style="list-style-type: none"> The range between the minimum toxic dose and the minimum therapeutic dose, or The range of doses over which the drug is effective for most of the population and the toxicity is acceptable.
Imp Concept	<ul style="list-style-type: none"> Therapeutic dose is related to Potency. Therapeutic index is a measure of Safety. (Low TI drugs require monitoring e.g warfarin) Therapeutic window = therapeutic Dose Range that safely and effectively treats disease.
Steady state concentration (Css)	<ul style="list-style-type: none"> Css occurs when the amount of a drug being absorbed is the same amount that's being cleared from the body when the drug is given continuously or repeatedly. Steady-state concentration is the time during which the concentration of the drug in the body stays consistent. At least 4-5 half lives are required to achieve Css in first order reactions. Css = dose × 4.5 half Lives. Css Depends upon half-life and unaffected by dose and dosing frequency. Example: Dopamine has half-life of 2 min. After 9 mins it will achieve steady state concentration
Loading dose	<ul style="list-style-type: none"> A dose of medication, often larger than subsequent doses administered for the purpose of Establishing a therapeutic level of the Medication. Primary purpose is to attain steady- State concentration of the drug as quickly as possible, usually right from the start of the dosage regimen for the treatment.
Maintenance dose	<ul style="list-style-type: none"> After the loading dose is given, another dose is given to maintain the Steady- state drug conc. /plateau. Such dose is known as maintenance Dose. i.e., to maintain the response of drug by replacing drug lost during dosing interval. In Renal/liver diseases – maintenance dose ↓ and loading dose is unchanged.

DRUG ANTAGONISM

One drug or inhibits action of another drug i.e., Effect of A + B < Effect of drug A + Effect of drug B.

Types of Antagonism

Physical Antagonism	<ul style="list-style-type: none"> Based on physical property of drugs, e.g., charcoal (adsorb alkaloid) in alkaloidal poisoning.
Chemical Antagonism	<ul style="list-style-type: none"> A type of antagonism where a drug counters the effect of another by simple chemical reaction / neutralization (not binding to the receptor). e.g., Calcium sodium edetate form insoluble complexes with arsenic / lead.
Functional Antagonism	<ul style="list-style-type: none"> Also known as Physiological Antagonism. Opposite effects of two drugs on same function, two drugs act on two different Types of receptors & antagonize action of each other e.g. Glucagon and insulin on blood sugar level.
Pharmacological Antagonism	<ul style="list-style-type: none"> Types: Competitive (may be reversible or irreversible): inhibitor binds at active site. e.g., Flumazenil by binding to BZD site antagonizes the effects of BZD by preventing the binding of GABA to GABA_A receptor. Non-competitive : inhibitor binds at allosteric or non-active site. Competitive Reversible : Effect can be reversed by inc drug concentration i.e. can be overcome by ↑ substrate. Vmax unchanged, ↑Kmax potency ↓ (high dose required), no effect on efficacy. Competitive Irreversible Antagonism Have affinity for the same receptor sites and bind by covalent bond. Effects cannot be overcome even by increasing the concentration of the agonist. Kmax unchanged, Vmax and efficacy ↓ Non-Competitive Antagonism Binds to site other than the agonist site Prevents the receptor activation by the agonist. The effect can't be overcome by inc agonist concentration. Example: Nor-epinephrine and phenoxybenzamine on alpha receptors Kmax unchanged, Vmax and efficacy ↓ (Same as Competitive antagonism) Examples of pharmacological antagonism: Atropine and Acetylcholine. Naloxone and Morphine at opioid-Receptors.

AGE RELATED CHANGES IN PHARMACOKINETICS	
Absorption	○ sInc gastric PH and delayed gastric emptying, absorption influenced by drug-drug/food interactions.
Distribution	<ul style="list-style-type: none"> ○ ↑ body fat content (↑ Vd for lipophilic drugs e.g propofol). ○ ↓ total body H₂O -- ↓ Vd for hydrophilic drugs e.g digoxin. ○ ↓ albumin – decreased binding for acidic drugs.
Metabolism	<ul style="list-style-type: none"> ○ ↓ hepatic mass, blood flow and metabolism. Phase 1 metabolism is lost with aging. ○ Lorazepam, oxazepam can be used in hepatic insufficiency.
Elimination	○ ↓ GFR and tubular secretion, increased plasma concentration of renally excreted drugs.
TYPES OF PHARMACODYNAMICS INTERACTIONS	
Additive (2 + 2 = 4)	<ul style="list-style-type: none"> ○ Effect of substance A and B together is equal to sum of their individual effects. 2 + 2 = 04 ○ Example : aspirin and acetaminophen
Synergistic (2 + 2 > 4)	<ul style="list-style-type: none"> ○ Effect of substance A and B together is greater than sum of their individual effects. 2 + 2 > 4. ○ Example : aspirin + Clopidogrel
Permissive	<ul style="list-style-type: none"> ○ Presence of substance A is required for full effects of drug substance B. ○ Example: Increased responsiveness of catecholamines by cortisol and thyroid hormones.
Potentialiation (2 + 0 > 2)	<ul style="list-style-type: none"> ○ Drug B with no therapeutic action enhances the effect of drug A. ○ For example, Carbidopa blocks decarboxylase to increase dopamine effects.
Antagonism (2 + 2 < 4)	<ul style="list-style-type: none"> ○ Effect of substance A and B together is less than sum of their individual effects. 2 + 2 < 4 ○ Ethanol antidote for methanol poisoning.
Tachyphylaxis	<ul style="list-style-type: none"> ○ Rapid or acute decrease in drug response after repeated or initial administration. ○ Develops rapidly and increasing the drug dose has no effect . ○ Example: Nitrates, niacin, ephedrine, hydralazine, phenylephrine, LSD and MDMA.
Tolerance	○ Diminution of drug response that develops slowly over longer periods of time and effect can be received after increasing the dose of drug e.g Barbiturates.
Idiosyncrasy	○ Genetically determined unusual or abnormal response to a drug and it follows dose dependent curve e.g Lignocaine, barbiturates chloramphenicol. Prior drug reaction history is not essential.
Hypersensitivity or drug allergy	<ul style="list-style-type: none"> ○ Reaction to a particular chemical in drug resulting from previous exposure to substance. ○ E.g skin rashes, anaphylaxis, bronchospasm etc. ○ Allergy Occurs mostly on 2nd dose in comparison to idiosyncrasy which happens on 1st dose.

Urine PH and Drug elimination	<ul style="list-style-type: none"> ➤ Ionized species are trapped in urine and cleared quickly. Neutral forms can be reabsorbed. ➤ pKa is the PH at which drug is 50% ionized and 50% non-ionized. ➤ Represents the strength of weak acid or base. ↓ pKa means ↑ acidic drug.
Weak acids	<ul style="list-style-type: none"> ➤ They are Trapped in basic media. ➤ Treat overdose with NaHCO₃ to alkaline urine e.g Aspirin, methotrexate, and phenobarbital.
Weak bases	<ul style="list-style-type: none"> ➤ Trapped in acidic environment. ➤ Treat overdose with NH₄ Cl to acidify urine e.g TCAs and amphetamines.

AUTONOMIC NERVOUS SYSTEM (ANS) DRUGS		
Parasympathomimetic or Cholinergic drugs (Activate the PSNS) ↑ ACh levels	<u>Direct agonists</u>	
	Bethanechol	B for bladder and Bethanechol. Used in urinary retention.
	Carbachol	Constricts pupil, used in Open angle glaucoma.
	Pilocarpine	Potent stimulator of tears, sweat and saliva, used in Xerostomia, open + closed angle glaucoma, tertiary amine--crosses BBB
	Methacholine	Used in challenge test for diagnosis for asthma.
	<u>Indirect agonists or Anti - cholinesterase</u>	
	Physostigmine	Crosses BBB (tertiary amine – not charged) Used as: antidote for anticholinergic poisoning e.g Atropine poisoning.
	Pyridostigmine	Quaternary amine (can't cross BBB), DOC for myasthenia gravis.
	Neostigmine	No CNS penetration (Quaternary amine +ve charged). Used in myasthenia, paralytic ileus, post-op reversal of NMJ blockade
	Edrophonium	Initial test used to diagnose Myasthenia gravis.
	Donepezil, rivastigmine, galantamine	First line for Alzheimer's disease.
	<u>Anticholinesterase poisoning (e.g., Organophosphate poisoning)</u>	
	Muscarinic effects	DUMBELSS = Diarrhea, urination, miosis, bronchospasm, bradycardia, emesis, lacrimation, sweating and salivation.
	Nicotinic effects	Neuromuscular blockade like succinylcholine. Tachycardia, twitches, muscle weakness, fasciculations.
	CNS effects	Respiratory depression, lethargy, Seizures, and, coma,
Parasympatholytics or Anticholinergics	<u>Treatment of Organophosphate Poisoning</u>	
	Atropine For reversal of muscarinic side effects + CNS symptoms (crosses BBB)	Pralidoxime – a specific antidote that regenerates AChE via dephosphorylation. Can't cross BBB, relieves nicotinic effects.
	<u>Muscarinic antagonists</u> : Atropine, scopolamine, glycopyrrolate, ipratropium.	
	<ul style="list-style-type: none"> ○ Atropine : causes mydriasis, bradycardia, decreases secretions. Used for reversal of symptoms in anticholinesterases poisoning e.g Organophosphate poisoning. ○ Side effects of atropine : Hyperthermia, flushing, angle closure glaucoma, dry mouth, and skin, blurred vision, headache, hallucinations, delirium etc. A famous toxidrome is : Hot as hare, mad as hatter, blind as bat, red as beet for toxicity of anticholinergics. ○ Scopolamine : used for motion sickness. It is sedative and causes euphoria also. ○ Atropine, homatropine, tropicamide → produce mydriasis and cycloplegia. ○ Glycopyrrolate : used IV pre-operatively to decrease secretions of airways. ○ Hyoscyamine, dicyclomine : antispasmodic for IBS. ○ Oxybutynin, Solifenacin, Tolterodine, Tropsium : used for reducing bladder spasms and urge urinary incontinence (overactive bladder). ○ Benztropine, trihexyphenidyl : used in Parkinson disease and for acute dystonia. 	
	<u>Ganglionic blockers</u> : nicotine, mecamylamine . Nicotine patch- used for smoking cessation	
	<u>Neuromuscular blockers</u> :	
	<ul style="list-style-type: none"> ○ Competitive (non-depolarizing) blockers : Atracurium, mivacurium, pancuronium rocuronium, all these are reversed by Neostigmine and cause no fasciculations. Atracurium releases Histamine (may cause bronchospasm). ○ Non-competitive (depolarizing) blockers : Succinylcholine. Rapid onset, short duration. Effects can't be reversed by neostigmine and may cause fasciculations. ○ Succinylcholine is Contraindicated in burns, Hyperkalaemia and malignant hyperthermia 	

Sympathomimetics or adrenergic drugs	<p>Direct acting: Epinephrine, NE, Dopamine, fenoldopam, isoproterenol, phenylephrine</p> <ul style="list-style-type: none"> ○ Epinephrine: $\beta > \alpha$ effects, DOC for cardiac arrest and anaphylactic shock. Used with local anesthetic agents (except the areas supplied by End arteries e.g. distal fingers). ○ Stronger effect at β_2 receptors. \uparrow HR \uparrow CO, (At high doses \uparrow BP). ○ Norepinephrine: $\alpha_1 > \alpha_2 > \beta_1$. \uparrow BP, \downarrow HR (reflex bradycardia) DOC for Septic shock. Can be used in hypotension. ○ Phenylephrine: $\alpha_1 > \alpha_2$, \uparrow BP, \downarrow HR. Used as mydriatic, decongestant in rhinitis, vasoconstriction leads to \uparrow BP ○ Dopamine: $D_1 = D_2 > \beta > \alpha_1$. \uparrow BP, \uparrow HR, \uparrow CO. ○ at low doses beta effects, DOC for Cardiogenic shock (inotropic), used in unstable bradycardia. At high doses \rightarrow alpha effects (vasoconstriction) ○ Albuterol, salmeterol: $\beta_2 > \beta_1$ agonists. Used in asthma. ○ Mirabegron: β_3 agonist used in urine urgency or overactive bladder. <p>Indirect acting: amphetamine, cocaine ephedrine. All are indirect general agonists.</p> <ul style="list-style-type: none"> ○ Amphetamine: used for ADHD, Narcolepsy. ○ Cocaine: cause vasoconstriction, coronary vasospasm and \uparrow \uparrow BP, used as local anesthetic agent and to diagnoses Horner syndrome. Cocaine may cause MI. ○ Ephedrine: causes euphoria, nasal decongestant, used by athletes to enhance performance. 				
Sympatholytic drugs	<table border="1"> <tr> <td data-bbox="472 835 613 1304"> Alpha blocker </td><td data-bbox="613 835 1479 1304"> <p>Non-selective blockers:</p> <ul style="list-style-type: none"> ○ Phenoxybenzamine and phentolamine block both alpha 1 & 2 receptors. ○ Phenoxybenzamine is used pre-operatively along with beta blocker in pheochromocytoma to manage B.P ○ Phentolamine is used for skin necrosis following vasoconstrictor use. <p>Selective blockers:</p> <ul style="list-style-type: none"> ○ Alpha 1 blockers : Prazosin, doxazosin, tamsulosin – used in BPH ○ Tamsulosin is specifically alpha 1a blocking agent (Maxflow) ○ Alpha methyl Dopa is alpha 2 agonist but acts as sympatholytic agent by decreasing CNS sympathetic outflow. Similarly, clonidine and guanfacine are alpha 2 agonist acting as sympatholytic agents. ○ Clonidine is used for diabetic diarrhea, euphoric, causes sedation. ○ Alpha 2 blockers: Yohimbine and Rauwolscine may be used for erectile dysfunction. ○ Alpha 2 blocker Mirtazapine may be used in depression and to \uparrow weight. </td></tr> <tr> <td data-bbox="472 1304 613 1543"> Beta blocker </td><td data-bbox="613 1304 1479 1543"> <p>Both alpha and beta blocking effects : Carvedilol, labetalol.</p> <p>Both β_1 and β_2 blockers or non-selective blockers: Prototype is Propranolol. Others are Pindolol, nadolol, timolol.</p> <p>Partial agonists : pindolol. Acebutolol – having intrinsic sympathetic role.</p> <p>Cardio-Selective (β_1 blockers) agents : atenolol, Betaxolol, Acebutolol. Metoprolol, bisoprolol. Bisoprolol can be given in asthma.</p> <p>Mortality benefit in HFrEF : carvedilol, Metoprolol, bisoprolol</p> </td></tr> </table>	Alpha blocker	<p>Non-selective blockers:</p> <ul style="list-style-type: none"> ○ Phenoxybenzamine and phentolamine block both alpha 1 & 2 receptors. ○ Phenoxybenzamine is used pre-operatively along with beta blocker in pheochromocytoma to manage B.P ○ Phentolamine is used for skin necrosis following vasoconstrictor use. <p>Selective blockers:</p> <ul style="list-style-type: none"> ○ Alpha 1 blockers : Prazosin, doxazosin, tamsulosin – used in BPH ○ Tamsulosin is specifically alpha 1a blocking agent (Maxflow) ○ Alpha methyl Dopa is alpha 2 agonist but acts as sympatholytic agent by decreasing CNS sympathetic outflow. Similarly, clonidine and guanfacine are alpha 2 agonist acting as sympatholytic agents. ○ Clonidine is used for diabetic diarrhea, euphoric, causes sedation. ○ Alpha 2 blockers: Yohimbine and Rauwolscine may be used for erectile dysfunction. ○ Alpha 2 blocker Mirtazapine may be used in depression and to \uparrow weight. 	Beta blocker	<p>Both alpha and beta blocking effects : Carvedilol, labetalol.</p> <p>Both β_1 and β_2 blockers or non-selective blockers: Prototype is Propranolol. Others are Pindolol, nadolol, timolol.</p> <p>Partial agonists : pindolol. Acebutolol – having intrinsic sympathetic role.</p> <p>Cardio-Selective (β_1 blockers) agents : atenolol, Betaxolol, Acebutolol. Metoprolol, bisoprolol. Bisoprolol can be given in asthma.</p> <p>Mortality benefit in HFrEF : carvedilol, Metoprolol, bisoprolol</p>
Alpha blocker	<p>Non-selective blockers:</p> <ul style="list-style-type: none"> ○ Phenoxybenzamine and phentolamine block both alpha 1 & 2 receptors. ○ Phenoxybenzamine is used pre-operatively along with beta blocker in pheochromocytoma to manage B.P ○ Phentolamine is used for skin necrosis following vasoconstrictor use. <p>Selective blockers:</p> <ul style="list-style-type: none"> ○ Alpha 1 blockers : Prazosin, doxazosin, tamsulosin – used in BPH ○ Tamsulosin is specifically alpha 1a blocking agent (Maxflow) ○ Alpha methyl Dopa is alpha 2 agonist but acts as sympatholytic agent by decreasing CNS sympathetic outflow. Similarly, clonidine and guanfacine are alpha 2 agonist acting as sympatholytic agents. ○ Clonidine is used for diabetic diarrhea, euphoric, causes sedation. ○ Alpha 2 blockers: Yohimbine and Rauwolscine may be used for erectile dysfunction. ○ Alpha 2 blocker Mirtazapine may be used in depression and to \uparrow weight. 				
Beta blocker	<p>Both alpha and beta blocking effects : Carvedilol, labetalol.</p> <p>Both β_1 and β_2 blockers or non-selective blockers: Prototype is Propranolol. Others are Pindolol, nadolol, timolol.</p> <p>Partial agonists : pindolol. Acebutolol – having intrinsic sympathetic role.</p> <p>Cardio-Selective (β_1 blockers) agents : atenolol, Betaxolol, Acebutolol. Metoprolol, bisoprolol. Bisoprolol can be given in asthma.</p> <p>Mortality benefit in HFrEF : carvedilol, Metoprolol, bisoprolol</p>				

Uses of beta blockers (BB)	<ul style="list-style-type: none"> ○ CVS : Metoprolol, carvedilol for Hypertension, Angina, MI, Heart failure, SVT, HOCM ○ Others uses : Thyroid storm/hyperthyroidism (propranolol) , glaucoma (Timolol), capillary haemangioma, Variceal bleeding -- nadolol, carvedilol.
Adverse effects of BB	<ul style="list-style-type: none"> ○ Bradycardia, bronchoconstriction (asthma), AV blocks (1st degree) ○ Erectile dysfunction, dyslipidemias (metoprolol) ○ exacerbation of Asthma/COPD, masked hypoglycemia.

Drugs To Avoid in Old Age (Beers Criteria)

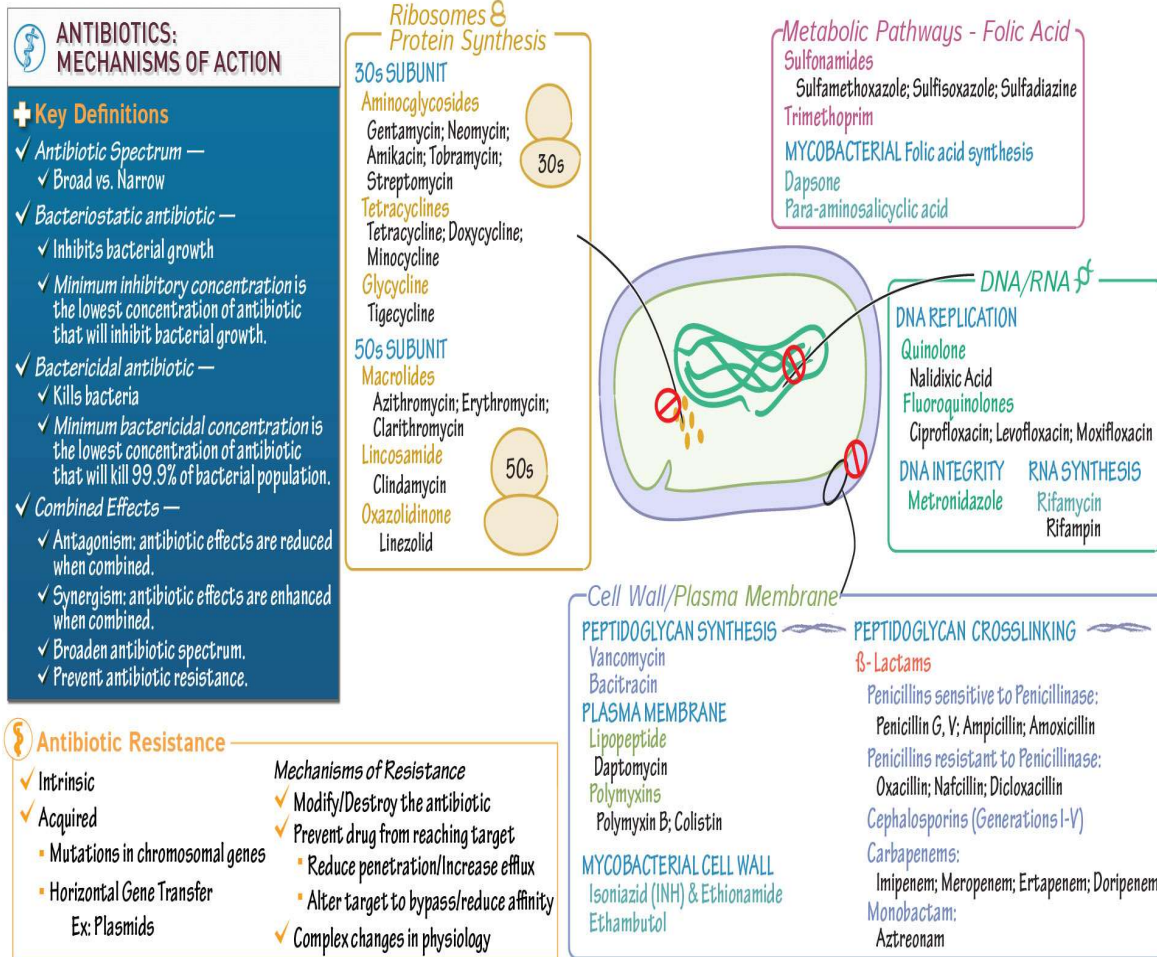
- Includes > 50 medications to be avoided in elderly due to low efficacy and increased risk of adverse effects in them.
- **alpha blockers:** high risk of hypotension
- **Benzodiazepines:** increased risk of delirium, sedation, and falls
- **NSAIDs:** risk of GI bleeding, especially with warfarin
- **PPIs:** increased risk of Pseudomembranous colitis by C.Difficile infection
- **Anticholinergics, antidepressants, antihistamines, opioids :** increased risk of constipation, urinary retention, falls, delirium, and sedation.

TOXICITIES AND SIDE EFFECTS OF DRUGS			
Toxicity	Drugs	Toxicity	Drugs
Nephrotoxic + ototoxic	Loop diuretics, Cisplatin, vancomycin amphotericin aminoglycosides, ,	Tendon and cartilage damage	Floroquinolones
Drug induced lupus	Procainamide , hydralazine, isoniazid, Phenytoin, sulfa drugs	Pseudomembranous Colitis (DOC is Metronidazole)	Ampicillin , clindamycin, PPIs, Floroquinolones Cephalosporins
Hyperuricemia or Gout	Pyrazinamide , thiazides, furosemide, niacin, cyclosporine	Megaloblastic anemia	Methotrexate , phenytoin, hydroxyurea
Osteoporosis	Corticosteroids , Heparin, PPIs	Thrombocytopenia	Heparin, quinidine, indinavir, linezolid
Teeth discoloration	Tetracyclines	Grey baby syndrome	Chloramphenicol
Gingival hyperplasia	Phenytoin , nifedipine	Red man syndrome	Vancomycin
Myopathy	Statins , steroids, daptomycin	G6PD related hemolysis	Primaquine , Dapsone.
Photosensitivity	Sulfonamides , amiodarone	Coomb's +ve hemolytic anemia	Methyldopa , penicillin, Cephalosporins
Fat redistribution	Protease inhibitors (Ritonavir)	Agranulocytosis	Clozapine , propylthiouracil
Hepatitis	Isoniazid, Rifampin, statins	Thrombosis	OCPs, HRT
Acute cholestatic hepatitis, jaundice	Macrolides e.g erythromycin	Pancreatitis	Didanosine , alcohol, steroids, azathioprine
Esophagitis	Bisphosphonates , NSAIDs	Hepatic necrosis	Halothane , Valproic acid, acetaminophen, Amanita
Diarrhea	Metformin , erythromycin, acarbose, ezetimibe, orlistat	Hot flashes	SERMs – Tamoxifen, raloxifene, clomiphene
Gynecomastia	Spironolactone , cimetidine, ketoconazole.	Hyperprolactinemia	Risperidone , haloperidol , metoclopramide
Hyperthyroidism	Amiodarone , iodine, lithium	Hyperglycemia	Steroids , protease inhibitors
Hypothyroidism	Amiodarone, lithium, Ethionamide	SIADH	Carbamazepine, SSRIs
Adrenocortical insufficiency	Sudden corticosteroids withdrawal leads to HPA suppression	Diabetes insipidus	Lithium, demeclocycline
Coronary vasospasm	Cocaine, Ergot alkaloids	Dilated cardiomyopathy	Doxorubicin , alcohol
Torsade's de pointes	Class IA and III antipsychotics Macrolides, ziprasidone	Parkinson like syndrome	Metoclopramide , reserpine Antipsychotics
Tardive dyskinesia	Antipsychotics , metoclopramide	Cinchonism (vision loss, tinnitus, hearing loss)	Quinine , Quinidine

Peripheral nephropathy	Vincristine , isoniazid, phenytoin, cisplatin	Idiopathic intracranial hypertension	Vitamin A toxicity , growth hormones, Tetracyclines
Color blindness	Ethambutol	Lens deposits	Chlorpromazine
Yellow vision	Digoxin	Retinal deposits	Theoridazine
Dry cough	ACE inhibitors (Captopril)	Corneal deposit/opacity	Chloroquine
Pulmonary fibrosis	Bleomycin, Busulfan, methotrexate	Fanconi syndrome	Cisplatin, tenofovir
Interstitial nephritis	Methicillin , PPIs, NSAIDs	Hemorrhagic cystitis	Cyclophosphamide
Disulfiram like reaction	Metronidazole , 1 st generation sulfonylureas, Griseofulvin	Antimuscarinic	Atropine, TCAs, H1 blockers, antipsychotics
Steven Johnson syndrome/Rash	Sulfonamides , anti-epileptic drugs, penicillin, allopurinol	Photosensitivity	Sulfonamides, amiodarone, tetracyclines

SPECIFIC TOXICITY TREATMENTS

Drug/Toxin	Specific Antidote	Drug/Toxin	Specific Antidote
ACHE inhibitors or OP poisoning	Pralidoxime – antidote Treatment – atropine > Pralidoxime	Warfarin	Immediate : FFPs Delayed : Vit K
Cyanide	Hydroxocobalamin, nitrates	Arsenic	Dimercaprol, succimer
Iron	Deferoxamine, deferiprone	Opioids	Naloxone
Lead	EDTA, Penicillamine, Dimercaprol	Methotrexate	Leucovorin
Mercury	Dimercaprol, succimer	Salicylates	NaHCO ₃ , dialysis
Copper	Penicillamine	TCAs	NaHCO ₃ (stabilizes cardiac cell membrane)
Antimuscarinic, anticholinergics	Physostigmine	Carbon monoxide	100% O ₂ , hyperbaric O ₂
Acetaminophen	N-acetylcysteine (replenishes glutathione)	Digoxin	Digi-Fab
Dabigatran	Idarucizumab	Methanol	Fomepizole
Methemoglobin	Methylene blue, vitamin C	Beta blockers	Atropine, glucagon, saline
Apixaban	Andexanet alpha	Heparin	Protamine sulfate



Bactericidal antibiotics	<ul style="list-style-type: none"> ○ They kill the bacteria i.e. irreversible damage. Examples include: ○ beta lactam agents, (Penicillins, Cephalosporins), vancomycin, aminoglycosides, Quinolones, bacitracin, polymyxins metronidazole, isoniazid, Rifampin, pyrazinamide, Daptomycin, streptogramins, linezolid
Bacteriostatic antibiotics	<ul style="list-style-type: none"> ○ They inhibit the growth (do not kill the bacteria). Examples are: ○ macrolides, Trimethoprim, Sulfonamides, tetracyclines, chloramphenicol, clindamycin, nitrofurantoin, Ethambutol.

SUMMARY + HIGH YIELD POINTS REGARDING ANTIBIOTICS

CELL WALL SYNTHESIS INHIBITORS	
○	Penicillins, Cephalosporins, carbapenems, Monobactams, vancomycin.
○	Penicillin G is DOC for N.meningitidis and T. Palladium. May cause Hemolytic anemia and interstitial nephritis.
○	Ampicillin is active against listeria. May cause C. Difficile infection – pseudomembranous colitis.
○	Dicloxacillin, nafcillin, oxacillin are active against S. Aureus except MRSA.
○	Piperacillin + ticarcillin are antipseudomonal Penicillins and they are also active against gram -ve rods.
○	5 generation of Cephalosporins,
○	Organism not covered by 1 st to 4 th generation Cephalosporins are LAME : Listeria, atypicals (Chlamydia, mycoplasma), MRSA, and Enterococci.
○	1 st generation cephalosporin cefazolin is used prior to surgery (e.g dental) to prevent S.aureus wound infection
○	2 nd generation (cefaclor, cefoxitin, cefuroxime, cefotetan) covers E.coli, H.infl, Neisseria, proteus, gram +ve cocci.
○	3 rd generation (ceftriaxone, cefixime, ceftazidime, cefotaxime) can cross blood brain barrier
○	Ceftriaxone for Meningitis, gonorrhoea, disseminated Lyme disease. Ceftazidime for pseudomonas.
○	4 th generation Cefepime covers pseudomonas and gram +ve organisms.
○	5 th generation (ceftaroline) covers MRSA, Enterococci, but not pseudomonas.
○	Cephalosporins may cause Vit K deficiency (bleeding), nephrotoxicity and disulfiram like reactions (flushing).
○	Mechanism of resistance for B-lactam antibiotics : alteration of penicillin binding proteins/transpeptidases.
○	Beta lactamase inhibitors: Clavulanic acid, avibactam, sulbactam, tazobactam. Augmentin = Amoxicillin + clavulanate
○	Carbapenems (Doripenem, imipenem, meropenem, ertapenem) cover gram + cocci, gram -ve rods, anaerobes.
○	They are always administered with Cilastatin (dehydropeptidase I inhibitor).
○	Meropenem doesn't require Cilastatin and has less risk of seizures.
○	Imipenem is the DOC for Actinobacter bumanii.
○	Monobactams (Aztreonam) covers gram -ve rods only, not activity against gram +ve rods or anaerobes .
○	Vancomycin covers MRSA, enterococci and orally given in C. Difficile infection, nephrotoxic and causes red man syndrome.
PROTEIN SYNTHESIS INHIBITORS	
○	Aminoglycosides, macrolides, Tetracyclines, tigecycline, chloramphenicol, clindamycin, Linezolid.
○	All of them are bacteriostatic except Aminoglycosides (bactericidal), linezolid -variable (bactericidal/static)
○	Binding to 30 S subunit : Aminoglycosides, tetracyclines, tigecycline (ATT).
○	Binding to 50 S subunit : Macrolides, Chloramphenicol, Clindamycin, Linezolid (MCL)
○	Aminoglycosides (Gentamycin, neomycin, tobramycin, streptomycin, amikacin) cover severe gram -ve rods infections e.g Pseudomonas (most active against it). They are synergistic with penicillin, cause misreading of mRNA, block translocation and inhibit initiation complex formation, require O ₂ for uptake – ineffective against Anaerobes.
○	Neomycin is used for bowel surgery. Don't ever give aminoglycosides to myasthenia gravis patient as they may cause NMJ blockade. Severely nephrotoxic and ototoxic.
○	Tetracyclines (Tetracycline, doxycycline, minocycline) cause discoloration of teeth and don't take them with Milk or iron containing preparations due to chelation effect. They are effective against atypicals (mycoplasma, chlamydia, rickettsia), salmonella typhi, malarial parasites and MRSA, also used for acne treatment. Doxycycline is excreted in faeces.
○	Tigecycline covers anaerobes, MRSA, VRE, Gram -ve and gram +ve.
○	Macrolides (erythromycin, azithromycin, clarithromycin) are used in atypical pneumonias (mycoplasma, chlamydia, legionella), STIs, gram +ve infections (in patients allergic to penicillin) and B Pertussis. They may cause diarrhea, jaundice, cholestatic hepatitis, rash, eosinophilia.
○	Chloramphenicol has limited use due to toxicity, can be used in typhoid , meningitis, UTI. It may cause dose dependant anemia and dose independent aplastic anemia. Gray baby syndrome is idiosyncratic reaction.
○	Clindamycin is active against anaerobes (Bacteroides, clostridium) in aspiration pneumoniae, lung abscess and oral infections. It treats anaerobic infections above diaphragm vs Metronidazole that treats anaerobes below diaphragm.
○	Clindamycin may cause pseudomembranous colitis, diarrhea and fever.
○	Linezolid covers gram +ve spp including MRSA & VRE. It may cause thrombocytopenia.
○	Polymyxins (colistin – polymyxin E, polymyxin B) cover multidrug resistant gram -ve bacteria e.g Pseudomonas, E coli. They are used for superficial skin infections.
Anti-Folate : Sulfonamides and Trimethoprim	
○	Sulfonamides (bacteriostatic) inhibit dihydropteroate synthase, bactericidal only when combined with trimethoprim.
○	They are active against Nocardia, Gram+ve and gram -ve organisms. They may cause G6PD def related hemolysis
○	Dapsone is structurally distinct to Sulfonamides , used in Leprosy and may cause G6PD def linked hemolysis.

○ Trimethoprim: inhibits dihydrofolate reductase , bacteriostatic, may cause hyperkalaemia, megaloblastic anemia.
○ Used in combination with Sulfonamides. For example, TMP-SMZ combination in ratio of (1:5) is used for typhoid, malaria, shigellosis, UTI, toxoplasmosis, pneumocystis pneumoniae.
○ Inhibit DNA Replication : Fluroquinolones.
○ They are bactericidal, inhibit DNA gyrase/Topoisomerase II and Topoisomerase IV, must not be taken with antacids.
○ active against gram-ve rods of GIT and urinary tract e.g DOC for Pseudomonal UTI, also given in malignant Otitis externa.
○ They may cause superinfection, tendon or cartilage damage if used in children/ before 18 years, headache, QT prolongation, diarrhea.
○ Also, may cause tendonitis or tendon rupture in elderly patients > 65 years of age taking steroids (prednisone)
○ Inhibit RNA Replication : Rifampin, inhibits RNA polymerase, used against TB and meningitis prophylaxis.
○ Damages DNA integrity : Metronidazole (bactericidal + anti-protozoal) forms toxic free radicals that damages DNA, treats giardiasis, amoebiasis, trichomonas vaginalis, anaerobes, alternated to penicillin in H. Pylori triple therapy.
○ It may cause disulfiram like reaction (flushing, tachycardia, hypotension) with alcohol and metallic taste.

Antimicrobials contraindicated in pregnancy	<ul style="list-style-type: none"> ○ Sulfonamides: kernicterus ○ Aminoglycosides: ototoxicity, nephrotoxicity. ○ Ribavirin: teratogenic ○ Fluroquinolones: tendon/cartilage damage. ○ Clarithromycin: toxic to foetus ○ Tetracyclines: discoloration of teeth, bone growth inhibition , ○ Chloramphenicol: Gray baby syndrome, ○ Griseofulvin: teratogenic.
Antimicrobial Prophylaxis	<ul style="list-style-type: none"> ○ Exposure to meningococcal infection : Ceftriaxone, ciprofloxacin, or Rifampin ○ High risk for endocarditis and undergoing Surgical or dental procedures : Amoxicillin. ○ History of recurrent UTIs : TMP-SMX ○ Malaria prophylaxis for traveller : Atovaquone-proguanil, mefloquine, doxycycline, ○ Primaquine, or Chloroquine (for areas with Sensitive species) ○ Intrapartum penicillin G or ampicillin : Pregnant patients carrying group B strep. ○ Erythromycin ointment on eyes: Prevention of gonococcal conjunctivitis in Newborn. ○ Prevention of postsurgical infection due to S.aureus: Cefazolin. ○ vancomycin if +ve for MRSA ○ Prophylaxis of strep pharyngitis in child with Prior rheumatic fever : Benzathine penicillin G/ oral penicillin V.
Prophylaxis in HIV/AIDS	<ul style="list-style-type: none"> ○ Pneumocystis pneumonia :TMP-SMX when CD4 < 200 cells/mm3 ○ Pneumocystis pneumonia and toxoplasmosis -- TMP-SMX when CD4 < 100 cells/mm3.

MIOTICS	MYDRIATICS
<ul style="list-style-type: none"> ✚ Opioids ✚ Parasympathomimetics (Pilocarpine) ✚ Organophosphates (OP) ✚ Pontine lesion and OP poisoning may lead to bilateral pinpoint pupils 	<ul style="list-style-type: none"> ✚ Anticholinergics : Atropine, TCAs, tropicamide, antihistamines, scopolamine. ✚ Direct Sympathomimetics : Phenylephrine and epinephrine. ✚ Indirect acting Sympathomimetics: Cocaine, amphetamines, LSD.

PAST PAPERS BCQs

1. Use 1% Permethrin for Scabies.
2. 5 % Permethrin for Pediculosis (Lice).
3. Ciprofloxacin can be used for:
4. Enteric fever + Pulmonary anthrax + Pseudomonas related UTI, DM with CKD, and chest infections.
5. Tinidazole given for: Amoebic liver Abscess.
6. Give Morphine in Terminal Cancer / MI Pain.
7. Methotrexate: In active RA, DMARD used.
8. Chronic Myeloid leukaemia: Hydroxyurea.
9. Ciprofloxacin > Norfloxacin (if asked -- antibiotic to be given in Traveller's diarrhea).
10. Staph Aureus infection: use Cloxacillin.
11. Acute attack of severe UC: IV Corticosteroids.
12. Malignant Pleural Effusion : intrapleural Tetracycline injection.
13. Trichomonas Vaginalis : Metronidazole.
14. Acute anaphylactic Reaction after Penicillin injection, drug to be used is Adrenaline.
15. in pregnancy A Fib with h/o MS : IV HEPARIN to be given.
16. Penicillin G is DOC for: Meningococcal Meningitis.
17. Use Lorazepam for : Nightmares.
18. Petit mal / absence seizure DOC : Ethosuxamide.
19. Tapeworm infestation DOC : Praziquantal.
20. For Cerebral Edema : use Mannitol – equally distributed in CSF.
21. For Herpes Simplex keratitis : Trifluridine
22. Excretion of penicillin is actively inhibited by probenecid.
23. Longest acting NM blocker is pancuronium.
24. Diazepam can cause IV thrombophlebitis.
25. Single injection of benzathine penicillin for strep pharyngitis.
26. Endogenous muscular relaxant are endorphins.
27. Diazepam relaxes smooth muscle by inhibitory action on interneurons.
28. <u>DOC for Travellers diarrhea:</u>
29. 1st Bismuth subsalicylate 2nd Loperamide 3rd Cipro and Norfloxacin, Cipro > Norfloxacin
30. Dicumarol side effect increased bleeding. Dicumarol is antagonist to Vit K
31. Dicumarol increases clotting time.
32. Drug which has irreversible effect on platelet function Aspirin.
33. Patient using drug chronically repeated monitoring of which is required because of low Therapeutic index.
34. Man starts vomiting during flight, drug to be given is cyclizine.
35. Rifampicin: dark / orange urine, Pyrazinamide : Gout Hyperuricemia.
36. Drug which reverses the hypotension caused by anaesthetic / epidural or sub dural Anaesthesia: Ephedrine.
37. Optic neuritis ethambutol : decreased visual acuity, colour blindness.
38. Highly selective for Cox 2 celecoxib > meloxicam, while highly potent Cox 2 inhibitor Meloxicam > celecoxib.
39. Safest drug in Elderly DM 2 is tolbutamide.
40. For obese best drug is Metformin. For non-obese best drug sulfonylurea.
41. A lady on antidiabetics now C/O weight loss drug responsible is Metformin.
42. Theophylline inhibits erythropoietin.
43. thiazide diuretic cause hypokalemia > hypercalcemia > hyperuricemia > hyperglycaemia.
44. Most fav side effect of thiazide diuretic : thrombocytopenia.
45. Enzyme inhibitor : "SECOND" → Sulphonamides, Erythromycin, Cimetidine, Omeprazole, Na valproate, Disulfiram.
46. Enzyme inducers → Carbamazepine, Phenytoin, Rifampicin, Phenobarbitone, Smoking.
47. To monitor warfarin INR > PT and to monitor heparin : APTT.
48. Low dose oestrogens cause hepatic adenoma.
49. Aspirin adverse effect in normal dose --- GI disturbance.
50. Aspirin overdose may cause tinnitus and hyperthermia.
51. Aspirin overdose after 12 to 24 hours -- respiratory alkalosis.
52. Aspirin overdose for days --- raised anion gap metabolic acidosis.
53. Drug induced SLE by Procainamide, Isoniazid, Phenytoin, Quinidine, Hydralazine.

54. Patient came to dentist, tooth extraction , k/c of Rheumatic HD , allergic to penicillin, to Avoid endocarditis what antibiotic should be given clindamycin.
55. Not a function of nitro-glycerine : decrease heart rate.
56. Vasodilator not causing increase in heart rate given in angina : metoprolol.
57. Toxicity of lithium with thiazide diuretic is pharmacokinetics interaction.
58. Reverse action of morphine on naloxone is pharmacodynamics.
59. Drug of choice for OCD = fluoxetine > clomipramine (documented).
60. Epinephrine increases blood flow to skeletal muscles.
61. Pseudomonas is most sensitive to ceftazidime > gentamycin. Least sensitive to fluoroquinolones.
62. Sometimes, there is no option of ceftazidime, so, choose gentamycin there.
63. DOC for pseudomonas is ceftriaxone. But use ciprofloxacin in case of UTI due to pseudomonas.
64. Familial tremors treatment propranolol> procyclidine.
65. Amitriptyline metabolism reduced when used with Cimetidine.
66. Penicillin given to prevent rheumatic fever and infective endocarditis.
67. Basic drug binds alpha glycoproteins, while acidic drug binds albumin.
68. Powerful vasoconstrictor cocaine -- inhibits release of NO.
69. Metabolism of drugs is increased by increasing liver enzyme.
70. Decrease gentamicin clearance in old age: decrease renal function.
71. Dec clearance of gentamycin in obese due to affected distribution.
72. More local anaesthesia concentration in blood in intercostal block.
73. Phenyl over alcohol anaesthesia preferred because of less painful.
74. All drugs transported across placenta by facilitated diffusion by carriers.
75. Amino acids and fatty acids also cross placenta by carriers.
76. Mifepristone acts through anti progestin (progesterone antagonist).
77. Drug preventing breast CA spread (metastasis) to liver tamoxiphen.
78. For Systemic fungal infection amphotericin.
79. Mechanism of action of steroid inflammation = phospholipase A2 inhibition.
80. Onset and direction of local anaesthesia depends upon tissue pH.
81. Fio2 safe level which doesn't cause Retrolental Fibroplasia = 1(Not affected by FiO2 levels).
82. Beta blockers given cautiously in thyrotoxicosis.
83. Side effect of halothane is bradycardia, malignant hyperthermia.
84. Angina worsens by theophylline.
85. Tachyphylaxis decrease in drug effects with repeated dose.
86. SSRI (fluoxetine) and TCA cause serotonin syndrome.
87. Alpha adrenergic receptors antagonist: doxazocin.
88. Pt taking propranolol developed increased PR interval cause drug induced heart block.
89. Compared to propranolol, atenolol is more likely to produce CNS effects.
90. DOC in urinary incontinence: oxybutynin.
91. Compared to propranolol, atenolol more like to produce CNS side effects.
92. Tetanospasmin produces effects by blocking synaptic inhibition.
93. To facilitate the action of atropine – TCAs block cholinergic effects.
94. Which of the following produces impairment of nerve condition after blocking sodium: Tetrodotoxin
95. Lady on epilepsy meds presents with thickening of gum and hirsutism. It caused by :Phenytoin.
96. Tocolytic agent raising blood sugar levels is terbutaline.
97. Contraindication of propofol : hypersensitivity.
98. Emergency delirium caused by ketamine.
99. Atorvastatin prevents progression of atheroma.
100. Digoxin toxicity worsened by Hypokalemia > hypercalcemia.
101. DOC for pseudomonas UTI which non lactose fermenting and oxidase positive : Ciprofloxacin.
102. Anticoagulants are contraindicated in thrombocytopenia.
103. Anticholinergics (ipratropium) used in COPD.
104. Diabetic female in pregnancy -- give insulin.
105. Herpes labialis treated by acyclovir.
106. Drug addict complaining of pain, give I/M ketorolac.

107.Maximum safe dose of bupivacaine : 150 mg.
108.Bupivacaine block voltage gated Na channels.
109.Succinylcholine toxicity may occur in individuals having deficiency of pseudocholinesterase.
110.Erythematous swelling on the back of hand: Give cloxacillin.
111.Which drug increases lower esophageal sphincter tone and speed up gastric emptying : Metoclopramide.
112.OFLOXACIN: for treating gonorrhoea and chlamydia.
113.Most common side effect of histamine 1 blocker : sedation.
114.Biguanides side effects --- diarrhea / flatulence , Lactic acidosis.
115.Drug causing peripheral neuropathy and pancreatitis : Didanosine.
116.Pt in ICU with CVP started having fever. Blood cultures showing gram positive cocci, drug to Give – Vancomycin.
117.Indication of furosemide acute pulmonary Edema.
118.Chance of bleeding in a patient with epidural, will be greatest in LMWH.
119.Edema reduced by diuretic due to secretion of sodium.
120.Nalbuphine is as potent as morphine.
121.Hyperthyroid lady with ventricular tachycardia pulse is 180/min, treatment of choice – Propranolol.
122.Analgesic causing tachycardia in therapeutic dose: Pethidine.
123.Good analgesic but weak anaesthetic agent is Nitrous oxide.
124.Effect of drug on body is its pharmacodynamics.
125.In hypovolemia with hypotension isoflurane should not be given why ?? it is a potent Vasodilator.
126.Antacid causing delayed gastric emptying is: Aluminium hydroxide.
127.During general anaesthesia halothane is given in combination with Nitrous oxide
128.A semiconscious patient is brought due to some drug intake , NaHCO ₃ administration Reverses the effect of that drug the drug is --- Phenobarbital.
129.Contraindicated in patient with raised intracranial pressure: ketamine.
130.OCPs are contraindicated in migraine.
131.Most dangerous adverse effect of valproic acid is fulminant hepatitis.
132.Succinylcholine action is prolonged due to deficiency of pseudo cholinesterase.
133.Opioid produce vomiting by acting on chemoreceptor trigger zone.
134.CSF with increased proteins and polymorphs with decrease glucose the drug of choice : Ceftriaxone
135.Type 3 antiarrhythmic drug is amiodarone (broad spectrum)
136.Pethidine preferred over morphine due to fast acting > less addictive.
137.Pethidine causes tachycardia in therapeutic dose.
138.Bupivacaine overdose adverse ventricular arrhythmias
139.Pt anesthetized heat will not be produced due to loss of muscle tone.
140.Side effects of chlorpromazine : dystonia
141.Transport of local anaesthetic across placenta by Simple diffusion
142.Drug used in endometriosis is medroxyprogesterone acetate.
143.Mode of action of cephalosporin inhibits transpeptidases.
144.Lithium is toxic antipsychotic when it should be stopped ? when coarse tremors develop in patient.
145.Lithium in normal doses cause fine tremors and toxicity (> 2 mmol/l) causes coarse tremors.
146.Lithium in toxic doses cause coarse tremors.
147.Which antiemetic preferred in patients of cancer : ondansetron (5-HT ₃ antagonist).
148.Ranitidine different from cimetidine as it has less CNS toxicity effect.
149.Aluminium hydroxide causes constipation ; Magnesium hydroxide causes diarrhea.
150.Edrophonium most common side effect : Nausea.
151.Bupivacaine first sign of overdose is ringing of ears.
152.Bupivacaine serious adverse effects : arrhythmias.
153.Alpha 2 agonist used in ICU is dexmedetomidine.
154.Most suitable NSAID during lactation is Ibuprofen.
155.Post partum lady with heavy bleeding due to uterine atony drug used would be Ergometrine.
156.Ergometrine is contraindicated in peripheral vascular disease.
157.Morphine reduces apnoeic threshold.
158.Indication of furosemide : Acute pulmonary Edema.
159.Erythematous swelling on the back of head treated with cloxacillin.

160. Ofloxacin for treating gonorrhoea and chlamydia.
161. Metronidazole is not a folate synthesis blocker.
162. Vancomycin inhibitor of proteoglycan
163. Metronidazole MOA: Damages DNA.
164. Chlorothiazide causes hyperuricemia >> Hyperglycemia >> hyperlipidaemia.
165. Cefazolin prevents staph aureus.
166. Lady treated for epilepsy with phenytoin now wants to get pregnant which antiepileptic is safer in pregnancy?? Carbamazepine >>> Phenobarbitone but in exam always click Phenobarbitone as Carbamazepine is not in options.
167. Ketamine causes bronchodilation.
168. Indirect bilirubin raised by methyl dopa.
169. Highest bioavailability of antiemetic metoclopramide.
170. Digoxin toxicity inc by loop diuretics.
171. Thrombocytopenia may occur by thiazide diuretic.
172. Bovine ultra lenti is long-acting insulin.
173. Pt with allergy of xylocaine may face mild syncope.
174. Ketamine contraindicated in intracranial HTN. Ketamine causes bronchodilation.
175. Which of the following narcotic when given epidural causes delayed respiratory Depression is fentanyl.
176. Corneal opacity chlorpromazine > chloroquine. Lens deposits : Chlorpromazine.
177. Single dose for streptococcal infection : Benzathine penicillin.
178. Most of the drugs are advised to take after meal to reduce gastric upset.
179. DOC for anaesthesia in patient with fits is thiopentone.
180. NM Blocker in a patient with Pheochromocytoma: pancuronium.
181. First FDA approved bio engineered drug : insulin.
182. Drug used in headache contraindicated in peripheral vascular disease Ergometrine.
183. Best way to manage febrile blood reaction are paracetamol.
184. Benzodiazepines cause hypotension in hypovolemic patient.
185. Calcium channel blocker acting on AV node verapamil – cardio selective.
186. Calcium channel blocker for both heart and vessels Diltiazem.
187. Calcium channel blocker for blood vessels – Nifedipine.
188. Effect of TCA starts as analgesic at 3 - 4 weeks.
189. Vitamin used for synthesis of CoA is pantothenic acid.
190. Use of terbutaline in preventing preterm labour causes hypoglycemia.
191. Taste changes metallic taste due to metronidazole
192. Drug via oral route having aqueous absorption digoxin.
193. Toxic effect of lignocaine -- prolonged seizures for 7-9 hours.
194. Toxic effect of lignocaine -- Prolong seizures for 9-7 hours.
195. Which effect caused by reduction of Cytochrome P450 Mechanism : Oxidation of phenytoin
196. Class 3 anti-arrhythmic amiodarone.
197. During fetal life kidney infected due to ACE inhibitors.
198. Shortest acting local anaesthetic : procaine ; Methemoglobinemia : Procaine > Prilocaine.
199. Common between diazepam and chlorpromazine : sedation
200. Chlorpromazine causes corneal deposits. Thioridazine causes retinal deposits.
201. Aspirin and other NSAIDs act on cyclooxygenase. Low dose aspirin inhibit TX A2
202. Penicillin excretion from kidney is decreased by probenecid.
203. Mechanism of action of methyl dopa is Inhibition of adrenergic system in CNS.
204. Thiazide decreases clearance of Lithium.
205. Antimetabolite used in cancer is methotrexate.
206. Drug given IV causes 60 % thrombophlebitis is diazepam.
207. Drug can be given preoperatively in a patient with liver decompensation is fentanyl.
208. Drug for Actinobacter humanii is imipenem.
209. Drug should be avoided in angina is theophylline.
210. ATT causing pins and needle sensation is isoniazid.
211. Injectable ATT which is nephrotoxic is amikacin.
212. Drug given in immunocompromised patients causing peripheral neuropathy and Pancreatitis is Didanosine.

213. Chlorpromazine exhibits anti-psychotic effects by action on dopamine.
214. Diff bet dexamethasone and hydrocortisone : dexamethasone causes less Na retention.
215. Scenario of pt. with congestive heart failure and pulmonary edema in acute distress Treatment -- IV furosemide.
216. Treatment of Enterococcus faecalis is Ampicillin.
217. Antipsychotic effect of phenothiazine is due to blocking dopamine receptors in limbic system.
218. Nifedipine causes refractory hypotension when given with halothane due to synergic effect on calcium channels.
219. Enterococcus faecalis is resistant to Ampicillin., although it also DOC for Ampicillin but Emergency resistant is noted against the drug for which vancomycin is used.
220. Drugs given in hypertrophic obstructive Cardiomyopathy is metoprolol (1 st line) verapamil (alternative)
221. Patient with hypotension should not give benzodiazepine in which case? hypovolemic
222. In a person with meningococcal meningitis and in the event of unknown allergy drug Given penicillin G.
223. DOC for pseudomonas: ceftazidime For UTI : Ciprofloxacin
224. Anti-hypertensive contraindicated in diabetic pt is propranolol → it may mask the symptoms of hypoglycemia.
225. Person on antiepileptic drugs now develop depression, drug used for depression with antiepileptic : fluoxetine (SSRI).
226. Naturally occurring alkaloids are morphine and codeine.
227. Patient came to local clinic with poisoning inhalation history upon examination you have noticed constricted pupils doctor gave naloxone, but the patient was not responding, the drug may be ? Phenobarbitone
228. Side effect of TCAs: general tonic clonic seizures
229. Pulmonary anthrax infection -- DOC Ciprofloxacin
230. DOC for obsessive compulsive neurosis is SSRI > clomipramine.
231. Therapeutic index of drug indicates Safety.
232. Patient having hypertension which Alpha Blocker to be given Doxazosin > tamsulosin.
233. DOC for pneumocystis Jirovecii -- TMP SMX.
234. Bacteriostatic Anti tuberculosis drug : Ethambutol.
235. Low dose heparin act by -- inhibiting factor Xa.
236. Most common drug used in nasal and sinuses fungal infection : amphotericin B (Mucor).
237. Patient comes with SVT which should be given verapamil.
238. Regarding Sucralfate cimetidine interaction: Sucralfate doesn't let cimetidine get Absorbed.
239. Most specific manifestation of penicillin hypersensitivity is bronchospasm.
240. Drug which causes bronchodilation through adenylyl cyclase : salbutamol
241. Psychiatric medication developing agitation and visual impairment is Thioridazine.
242. Cabergoline D 2 agonist: high affinity
243. A female patient has chronic hypertension started ACE inhibitors, BP controlled, but Dizziness cause: decreased blood supply to brain due to Decrease sympathetic tone.
244. ACE inhibitors contraindicated in renal disease. ACE inhibitors beneficial in DM
245. Metallic taste of the drug with GI disturbance Metformin ; Nasopharyngitis caused by : Sitagliptin.
246. MOA of IV potassium -- Na/K pump
247. Acetaminophen in urine is due to which modification glucuronidation.
248. Glucuronidation causes urine to appear in urine.
249. Pseudomembranous colitis is treated by Mild to moderate oral metronidazole.
250. If Severe oral Metronidazole plus oral Vancomycin.
251. Which antibiotic is present in saliva : erythromycin.
252. Bioavailability is the amount of active drug reaching blood.
253. Antibiotic reaching in saliva is erythromycin.
254. Which opioid causes fatal excitation with MAO inhibitors ? Pethidine.
255. Therapeutic dose of drug in clinics is decided based on potency.
256. Ketamine will cause myocardial depression if the pt has already been given propranolol.
257. Potency of local anaesthetic depends upon lipid solubility.
258. Regarding steep dose concentration small change in concentration will have greater Effect in response
259. Which drug does not cross blood brain barrier ? dopamine ; Levo DOPA crosses BBB.
260. DOC to treat endometriosis danazol.
261. Tramadol is a weak Mu agonist.
262. HTN female in OPD with indirect hyperbilirubinemia is methyl dopa.
263. Asthmatic pt had a cholecystectomy, now complaining of pain at site of surgery, analgesic suitable is ? Paracetamol

264. Most common side effect of diazepam when used in labour Neonatal Hypotonia
265. Halothane anaesthesia given to patient before surgery his temp rises because of Malignant hyperthermia due to skeletal muscles contraction.
266. Drug to be stopped 24 hours before surgery to prevent lactic acidosis is --- Metformin
267. Shortest acting beta blocker is esmolol.
268. Analgesic which has a bronchodilation effect is ketamine.
269. Side effect of dicumarol : increased Clotting time.
270. Minimal GI upset : paracetamol ; Max GI upset --- aspirin.
271. Digoxin -Given in: A Fib, SVT, CCF, flutter ; contraindications : obstructive cardiomyopathy, high Output CF
272. Barbiturates given in kernicterus , refractory status Epilepticus ; Contraindicated in Acute intermittent porphyria.
273. Non barbiturate hypnotic drug ? Bromide
274. Salicylate excretion increased by -- I/V NaHCO ₃
275. Skin disinfection : alcohol with chlorhexidine
276. Fluoxetine -not epileptogenic
277. Amitriptyline and imipramine are epileptogenic.
278. Ergotamine contraindicated in heart disease and HTN.
279. Digoxin toxicity increased by : Hypokalaemia > Hyper Ca > ,alkalosis.
280. Morphine given ,relieve pain in hours ? 3-4.
281. Naloxone reverses Resp depression & coma in? 30sec
282. Cough during induction of anaesthesia. Which drug Was given – Sevoflurane.
283. Which 1 is synthetic mineralocorticoid ? Fludrocortisone
284. Haemophilic pt with pain . Safe Analgesic ? Acetaminophen
285. Dimethyl diazepam half-life ? 32-200 hrs
286. Which is more pungent? Desflurane
287. Ketamine :A bronchodilator, Contraindication : intracranial HTN , Hallucination due to ketamine treated with ? Atropine Given I/M in cardiac surgery.
288. Mushroom poisoning : atropine
289. Drug used with methotrexate to reduce its s/e ? Leucovorin
290. Girl with severe ulcerative colitis, drug to give is I/V Steroids
291. MgSO ₄ antidote is CA gluconate.
292. Intrinsic heart rate determined by I/V atropine + atenolol.
293. Warfarin effect increased by?? Cimetidine
294. Man with pinpoint pupil not responding to naloxone is Phenobarbitone.
295. Therapeutic dose is measured by Potency.
296. Bioavailability determines Efficacy.
297. Basic drug binds to alpha glycoproteins
298. Following drugs promote each other's action ? Atropine and amitriptyline
299. Pt taking MAO inhibitors ,given barbiturates ,what will Happen ? Coma
300. Pt on MAO inhibitors with coffee, risk of HTN is there.
301. Cotrimoxazole given , C/o red urine ; Diagnosis ? G6pd deficiency
302. Drug with atropine like action is Scopolamine.
303. Digoxin toxicity increased by Hydrochlorothiazide.
304. Gastric emptying decreased by aluminium sulphate -- AlSO ₄ .
305. Drug contraindicated in CLD is Pentazocine
306. Drug to give in Herpes keratoconjunctivitis : Trifluridine.
307. Prinzmetal angina: give Diltiazem.
308. Pregnancy induced HTN (PIH): give labetalol > Methyldopa.
309. Pseudomonas infection: ceftazidime, cefepime, Cipro/ofloxacin , piperacillin/ ticarcillin , Aminoglycosides
310. Rib fracture : give bupivacaine.
311. Mountain sickness : acetazolamide.
312. Motion sickness : scopolamine ,cyclizine
313. Asthmatic pt muscle relaxant to give is Suxamethonium.
314. Asthma + IHD pt in OT ,to treat HTN ? I/V Nitro-glycerine.
315. Metastatic pleural effusion: bleomycin.

316.DOC ac pancreatitis :pethidine (analgesic).
317.Terminal CA pt : morphine (analgesic).
318.Diabetic + post op gastroparesis : metoclopramide (D2 antagonist).
319.Antiemetic for cancer chemotherapy : ondansetron (5 HT3 antagonist).
320.Anti-psychotic induced Parkinsonism: treat with Anticholinergic (benztropine).
321.Diabetic macular edema : ranibizumab
322.Known CCF pt presents with ectopics ,DOC ? Diuretics (treat HF it will Dec ectopics).
323.Pt with chest pain & ventricular ectopics DOC is Lidocaine [(it's the DOC for any kind of ventricular Arrhythmias after myocardial Ischemia (evident here with chest pain))]
324.Ventricular tachycardia after IHD : give I/V lidocaine.
325.DOC for A Fib : digoxin
326. Hypertrophic obstructive CM . which ca channel Blocker to use ? Verapamil ; Remember 1st line is Beta Blocker
327.Recurrent TIAs : use aspirin (if intolerant, ticlopidine)
328.Anaphylactic shock DOC : epinephrine
329.Acute asthma DOC : terbutaline (b2 agonist)
330.Partial absent seizures : Ethosuxamide
331.Status epilepticus DOC to start with ? Lorazepam
332.DOC systemic fungal infection :amphotericin
333.E.coli UTI DOC ? Ciprofloxacin
334.Drugs to be given in Hep C : IFN & ribavirin
335.Subarachnoid hemorrhage treatment: nimodipine
336.DOC CMG chorioretinitis : Ganciclovir
337.Hookworm /pinworm : mebendazole
338.Gynaecomastia : Griseofulvin ,digoxin ,cimetidine ,spironolactone
339.Reflex tachycardia : nitro-glycerine, CA channel Blockers, pethidine > morphine
340.Mild CCF monotherapy ? ACE inhibitor / Captopril
341.CCF with IHD : diuretics + ACE inhibitor
342.In Recurrent MI: give anticoagulants
343.DOC for ac ventricular failure with Resp distress : IV Furosemide. Acute LVF ,DOC ? I/V furosemide
344.Pt with CCF ,presents with arrhythmias ,DOC ? Digoxin
345.Amiodarone : thyroid dysfunction
346.Vancomycin :red man syndrome
347.Clindamycin : pseudo membranous colitis
348.Trimethapan : urinary retention in elderly
349.Nitro-glycerine : throbbing headache
350.Lithium carbonate : polyuria
351.Analgesic nephropathy features : haematuria ,sterile Pyuria
352.Thiabendazole causes : cholestatic jaundice.
353.Paracetamol poisoning : Renal papillary necrosis
354. Drug prescribed for HTN caused postural Hypotension ,diarrhoea, problem in ejaculation ,drug was ? guanethidine
355.Eye drops given caused severe pain ,reduced Vision ,drug given ? Atropine
356.Drug given for severe headache & vision Impairment ,pt developed dyspnea, drug ? Propranolol
357.Agranulocytopenia caused by phenytoin, clozapine
358.Methemoglobinemia : procaine ,B
359.Drugs safe in pregnancy (diff MCQs): Fluoxetine , Phenobarbitone, Co-Amoxiclav
360.Drugs crossing placenta : Morphine phenytoin diazepam
361.Penicillin: cell wall synthesis inhibitor. Tetracycline: inhibit protein synthesis. Rifampicin: inhibit transcription
362.Azathioprine: inhibit cellular and cytological immune responses.
363.Cyclosporine: blocks T cell differentiation blocks T cell maturation dec host response to graft.
364.Labetalol: alpha + beta blocker
365.Clonidine: centrally acting antihypertensive, presynaptic alpha 2 agonist in vasomotor Centre of brain, decreases sympathetic outflow
366.MOA of Steroids: Inhibit phospholipase A 2
367.Sulphonamides: inhibit tetrahydrofolate in bacteria

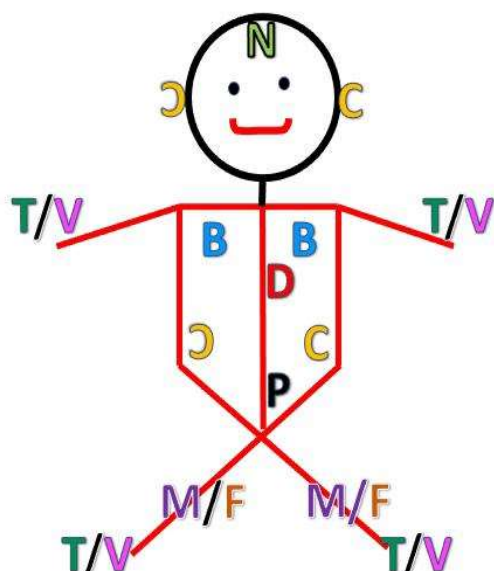
368. Na cromoglycate: Mast cell stabiliser
369. Neb with ipratropium: Decreases Ach release in bronchi.
370. Furosemide – Rapid diuresis
371. Curare: inhibit nicotinic Ach receptors
372. Aspirin: Irreversibly blocks COX
373. Morphine: Releases histamine
374. Heparin: inhibits clot propagation (not clot organisation)
375. EPO acts on stem cells (not CFU)
376. Digoxin increases contractility and decreases heart rate.
377. Side effects (asked one)
378. Phenylbutazone causes: Aplastic anemia.
379. Streptomycin: ototoxic /hearing loss
380. Aminoglycosides: ototoxic
381. Dipyridamole given in -- coronary steal syndrome.
382. Phenytoin side effects: Granulocytopenia, hirsutism, gingival hyperplasia, Interstitial Pneumonitis, drug Induced SLE, Ataxia, megaloblastic anemia (folate depletion), painful swollen gums.
383. Methotrexate side effects: Hepatotoxic, pulmonary Fibrosis, megaloblastic anemia
384. Lithium side effects: Hypothyroidism, renal toxicity, cardiac conduction abnormalities, nephrogenic DI, Gastric distress, tremors, Narrow therapeutic index. Stop Li when coarse tremors develop.
385. ACE Inhibitors: Bone marrow depression, neutropenia
386. Sulphonamides causes G6pd def -> Hemolysis, kernicterus, Nephrotoxic.
387. Opioid poisoning: Respiratory depression
388. Aminoglycosides: Both renal & ototoxicity
389. Bupivacaine is: Cardiotoxic.
390. Trazodone causes: Priapism
391. Terbutaline: Acidosis, Fine tremors
392. Azathioprine: given in Hepatosplenic T cell Lymphoma
393. Haloperidol: Neuroleptic malignant syndrome
394. Na valproate: Flexing tremor
395. Lithium carbonate: Polyuria
396. Drug of choice for open angle glaucoma: timolol, β_1 and β_2 blocker
397. Allopurinol: inhibits xanthine oxidase
398. Isoniazid: causes pyridoxine deficiency leading to peripheral neuropathy and Sideroblastic anemia, MOA: INH is nicotinic acid derivative that inhibits synthesis of Mycolic acid in mycobacteria cell wall
399. Succinylcholine : - depolarizing agent used as muscle relaxant during surgery, . binds to Nicotinic receptors in skeletal muscle causing persistent depolarization at motor endplate, Hydrolyses plasma cholinesterase, . initial fasciculation followed by muscle paralysis, duration of action only -10 min, effects not reversed by cholinesterase inhibitors- no Pharmacologic antidote to overdose, . some patients have atypical cholinesterase and cannot metabolize the drug.
400. Preganglionic neurotransmitter acetylcholine -- activates muscarinic and nicotinic Receptors, . muscarinic effects- pupillary miosis (contracts iris sphincter, used after Cataract surgery), accommodation of lens for near vision (contracts ciliary muscles), Bronchoconstrictor, slow heart rate (SA node effect), increase PR interval (AV nodal Effect), stimulate GI secretions and motility, micturition (stimulate detrusor muscle, which relaxes internal sphincter)
401. Nitric oxide: potent vasodilator synthesized in endothelial cells, activates cyclic GMP, which inactivates myosin light chain kinase in smooth muscle cells leading to Vasodilatation, Ach can lead to its synthesis when injected into vessels.
402. Woman in third trimester has premature contractions: use terbutaline, a selective β_2 - Adrenergic receptor agonist that inhibits uterine contractions.
403. Know effect of aspirin on kidney: . decrease PGE: synthesis (vasodilator) leading to Unopposed AT II effect \square renal papillary necrosis.
404. methotrexate : blocks dihydrofolate reductase ; causes Interstitial fibrosis in lungs.
405. Peripheral neuropathy and cancer drug causing it : vincristine.
406. Effect of mixing statin drugs with niacin: rhabdomyolysis – each drug by itself can Produce rhabdomyolysis.
407. MOA of amphotericin B: - binds ergosterol in fungal cell membrane, which increases its Permeability, - nystatin has same mechanism.
408. MOA of clotrimazole: inhibits ergosterol synthesis, . other azoles compounds have Similar action
409. MOA of flucytosine: inhibits nucleic acid synthesis

410.MOA of Griseofulvin: inhibits microtubule function and mitosis
411.Propylthiouracil: - drug of choice for decreasing synthesis of thyroid hormone in Graves' Disease, may causes agranulocytosis, only drug that can be used in pregnancy
412.Fastest way to increase heartbeat in shock: e order of drugs with decreasing Effectiveness is isoproterenol, dobutamine, and dopamine, . dopamine in low doses is renal Vasodilator.
413.Propylthiouracil: drug of choice for decreasing synthesis of thyroid hormone in Graves
414.Dapsone: sulfone that inhibits synthesis of folic acid by M. Leprae, may precipitate Haemolytic anemia in G6PD deficiency, Nephrotic syndrome, peripheral neuropathy
415.Prolongation of QRS on ECG: quinidine may cause it
416. Anticonvulsant/antiepileptic drug with effect on epiphyseal plate: phenytoin via its Revving up of the cytochrome system in the liver and causing vitamin D deficiency .
417. (increased metabolism of 25 hydroxylated vitamin D)
418.MOA of ondansetron: - selective serotonin 5-HT3 receptor antagonist, e useful in Blocking chemoreceptor trigger zone (CTZ) in the area postrema, hence preventing Vomiting
419.Heparin: MCC of thrombocytopenia in hospital
420.Acute Rx for coumarin overdose: fresh frozen plasma best choice
421.Nitrofurantoin: concentrated in urine, . urinary tract antiseptic for UTI.
422. Cyclophosphamide S/E: • hemorrhagic cystitis, transitional cell carcinoma, . activated (not Metabolized) in the liver.
423.Doxorubicin and prednisone: metabolized in liver.
424.Gout after cancer therapy: prevent by giving allopurinol to prevent gout and urate Nephropathy.
425.Muscle fasciculations after neuromuscular block: initial effect of succinylcholine.
426.MOA of levodopa: blocks peripheral dopa decarboxylase.
427.Bronchial asthma: . terbutaline can be used as bronchodilator, but albuterol more often Used.
428.Rx of paroxysmal supraventricular tachycardia: adenosine, including its association With WPW syndrome.
429.Captopril: . bradykinin side-effects include cough and angioedema, . cough not seen with losartan.
430.Hydralazine: better tolerated in fast acetylators, cause of drug induced SLE, .
431.Patient with hypertension, hypernatremia, and hypokalemia: give losartan, an ATII.
432.Receptor antagonist, is the best drug, corrects HIN and electrolyte problem (blocks Release of aldosterone, hence sodium is lost in the urine and potassium retained)
433.Rx of opioid overdose: naloxone, which is a competitive opioid receptor antagonist.
434. Urinary retention in prostate hyperplasia: - use selective alpha blockers, relaxes smooth Muscle in bladder neck and prostate, examples- prazosin, terazosin. (Alpha receptors are abundant in bladder neck and prostate).
435.Narcolepsy: Rx with amphetamines
436.Premature labour and must deliver baby: give glucocorticoids (betamethasone) to increase surfactant Synthesis.
437.Drug used to eliminate calcium in patient with hypercalcemia: loop diuretic.
438.Drug used to remove calcium from urine in a Ca stone former: Hydrochlorothiazide.
439.Patient with respiratory alkalosis and then metabolic acidosis: salicylate intoxication
440.S-phase drug used in treatment of acute lymphoblastic leukaemia: methotrexate.
441.Analog of hypoxanthine requiring HGPRTase for bioactivation: . 6-mercaptopurine,
442.Allopurinol could cause toxicity, since the drug is a purine
443.Drug that competes with dUMP for thymidylate synthase: 5-fluorouracil
444.Drug used in Rx of Wilm's tumor: actinomycin D (dactinomycin)
445.Antimetabolite that together with an antibiotic is used in Rx of acute myelogenous Leukaemia: cytarabine + daunomycin (anthracycline antibiotic)
446. Nephron site responsible for ACE inhibitors causing increase in serum creatinine: Block in AT II (works as vasoconstrictor of efferent arteriole in glomerulus) by ACE Inhibitor removes important control for maintaining intrarenal blood flow causing Potential for renal failure (particularly with bilateral renal artery stenosis).
447.Nephron site of action of thiazides: Na'/Cl pump in cortical thick ascending limb
448.Aminoglycosides affect the 30S ribosomal subunit.
449.prolonged QT interval with sotalol, amiodarone, " prolonged PR Interval with digitalis, B-blockers, . calcium channel blockers, giant U wave with Quinidine,
450.ST depression with digitalis (hockey stick configuration), quinidine, .
451.Short QT interval with digitalis, flat T wave with quinidine, bradycardia with quinidine
452.For 30S protein synthesis inhibitors (tetracyclines, aminoglycosides, spectinomycin)
453.Patient with Salmonella and G6PD deficiency: avoid TMP/SMX (sulphur drug)

454.MOA of disulfiram reaction with metronidazole -- inhibits aldehyde dehydrogenase.
455.MOA of Norfloxacin: inhibits DNA gyrase.
456.Avoid tetracycline in pregnancy.
457.MOA of erythromycin - inhibits 50S ribosomal subunit in bacterial protein synthesis.
458.Chloramphenicol S/E : aplastic anemia in adults (idiosyncratic, not dose dependent)
459.Child eats honey and gets weak: . botulism, . intestinal colonization of organism with Toxin production
460.Antihypertensive increasing blood lipids: - β -blockers, thiazides
461.MOA of trimethoprim: blocks dihydrofolate reductase
462.Muscle relaxant for electroconvulsive Rx: succinylcholine
463.Rx of prostate cancer: - leuprolide- GnRH agonist blocks FSH and LH and lowers
464.Testosterone and DHT, . flutamide- competes with testosterone for androgen receptor,
465.Finasteride- blocks 5 α -reductase, decreases DHT, increases testosterone (good for Preventing impotency and hair growth), mainly used in prostate hyperplasia,
466.Ketoconazole- reduce testosterone synthesis, more often used in hyperplasia.
467.Young woman with vaginal cytology containing malignant cells: DES exposure with Clear cell adenocarcinoma.
468.CMV infection: ganciclovir first, then foscarnet if it does not work.
469.Most common side-effect of immunosuppressant drugs: . infection, Squamous Cancer of skin MC cancer
470.EEG in patient with absence seizures: . shows 3/sec spike and wave Discharge, increased with hyperventilation.
471.Drug abuser with flu-like syndrome, fever, mydriasis: methadone + naloxone
472.Patient with polyuria, polydipsia: taking lithium- produces nephrogenic diabetes Insipidus.
473.Rx of ADHD: methylphenidate
474.Effect of chronic use of a hypnotic drug to induce sleep: psychological dependence.
475.Patient with Wegener's granulomatosis has hemorrhagic cystitis: cyclophosphamide Effect.
476.K1 is the active form of vitamin K.
477.Patient with hypertension has SLE-like syndrome: drug responsible is hydralazine.
478.woman's ring finger with blue discoloration on undersurface and H/o of Drug abuse and frequent sexual activity: probable IV heroin abuser using finger as site of injection that is for selling the drugs.
479. Hydroxychloroquine : . used in Rx of rheumatoid arthritis, . complications- retinal Degeneration, dermatitis, bone marrow depression
480. Penicillamine : - used in Rx of rheumatoid arthritis, complications- aplastic anemia, Renal damage (membranous glomerulonephritis)
481.Acetaminophen: weak cyclooxygenase inhibitor in peripheral tissues- lack of Ant inflammatory effect, . effector inhibitor of prostaglandins in CNS- antipyretic, Analgesic
482. Ribavirin MOA : inhibits guanosine triphosphate formation, which prevents capping of Viral RNA, . blocks RNA-dependent RNA polymerases, . used in Rx of RSV Infections
483. Tamoxifen : . estrogenic receptor partial agonist- blocks binding of oestrogen to receptors of estrogen sensitive breast cancer cells, . used primarily in breast cancers that are ER Positive, . also used in progesterone resistant endometrial cancer, . protects against Osteoporosis and increases HDL, complications- hot flashes like menopause: Vaginal bleeding endometrial hyperplasia / cancer.
484.HMG-CoA reductase inhibitors: . statin drugs block CH synthesis, hepatocytes Compensate by up-regulation of LDL receptor synthesis leading to increased clearance of IDL and LDL remnants derived from VLDL
485. Sildenafil : - drug for Rx of erectile dysfunction, - inhibits breakdown of cGMP by type 5 Phosphodiesterase – increases levels of cGMP, which causes vasodilatation in corpus Cavernosus and penis
486. Nitro-glycerine MOA : release nitric oxide (vasodilator) in endothelial cells, . primarily a Venodilator- causes venous pooling and reduces preload, .has some arterial Vasodilatation when administered - reduces afterload, used in angina, Acute Myocardial infarction/ACS.
487. Naproxen : newer, long-acting NSAID that blocks cyclooxygenase, . very significant Potential for renal damage in those with pre-existing renal disease
488.Stage fright anxiety: give propranolol.
489.B-2 agonists: activate adenylate cyclase to increase cAMP.
490.Girl on Rifampin becomes pregnant while on birth control pills: Rifampin up the Liver cytochrome system, like alcohol, barbiturates, phenytoin.
491.Drugs affecting tubulin in mitotic phase: vinca alkaloids, . paclitaxel
492.Drug for Smoking Cessation : Bupropion
493.Neuroleptic Malignant syndrome : Bromocriptine + Dantrolene

494.Serotonin syndrome : use Cyproheptadine
495.Excessive Vaginal delivery following delivery : Use Ergotamine
496.Microcytic Hypochromic anemia (Fe def anemia) : give IV IRON DEXTRAN
497.Doc For Septic Shock : Nor Adrenaline
498.Doc For Cardiogenic Shock : Dopamine > Dobutamine
499.Doc For Anaphylactic Shock & Cardiac Arrest : I/M Adrenaline
500.Doc For Unrecordable B.P In Hypovolemic Shock : 1st Give Adrenaline, Then, Dopamine.
501.Doc For Unrecordable B.P In Cardiogenic Shock : Dopamine

Chemo Man



- B:** Bleomycin, Busulfan
Pulmonary fibrosis
- C:** Cisplatin, Carboplatin
Nephrotoxicity & Ototoxicity
- D:** Doxorubicin
Cardiotoxicity
- M/F:** Methotrexate, 5-Fluorouracil
Myelosuppression
- N:** Nitrosoureas (lomustine, carmustine)
Neurotoxic (crosses BBB)
- P:** Cyclophosphamide
Hemorrhagic Cystitis
- T:** Taxanes (paclitaxel, docetaxel)
Peripheral neuropathy
- V:** Vinca alkaloids (vincristine > vinblastine)
Peripheral neuropathy

LYMPHATIC SYSTEM

(Important Points + past papers BCQs have been highlighted)

Lymph	<ul style="list-style-type: none"> ✚ Transparent Yellowish and Alkaline Liquid ✚ Derived From Tissue Fluid and Found in Lymphatic Vessels. ✚ 5gm/dl Protein Is Present in Lymph ✚ 120ml Of Lymph Flows in Blood. ✚ 100 mL By Thoracic Duct + 20 mL By Right Lymphatic Duct ✚ Lymphatics are Absent In CNS, Cornea, Bones, Lung Alveoli and Superficial Skin.
Thoracic Duct (Or) Left Lymphatic duct	<ul style="list-style-type: none"> ✚ 45cm Length. Main lymphatic duct and drains 75% of Body Lymph. ✚ Begins as dilatation of Cisterna Chyli anterior to L2 vertebrae ✚ Receives lymph from Left Upper Limb, left Head and Neck, Chest, and entire body inferior to ribs. ✚ Drains Lymph via Left Subclavian Vein. It Has valves & empties as follows (sequence wise) <ul style="list-style-type: none"> ○ Venous system near the union of left internal jugular and left subclavian vein. ○ Left venous angle. ○ Lt Brachiocephalic Vein.
Right Lymphatic duct	<ul style="list-style-type: none"> ✚ Formed by Union of Right Jugular, Subclavian and Broncho mediastinal trunks ✚ Receives Lymph from Right Head & Neck and Right Upper Limb. ✚ Ends by entering the right Venous angle.
Lymphatic Flow	<p>Lymph Capillary → Lymphatic Vessel → Lymphatic Node → Vessel → Lymph Trunk → Subclavian Vein</p> <p><u>Regulation Of Lymphatic Flow:</u></p> <ul style="list-style-type: none"> ✚ Mainly Depends Upon Muscular Massage and Arterial Pulsations. ✚ It also Depends on Intrathoracic Pressure and Interstitial Pressure ✚ Foot Massage Increases Lymph Flow ✚ Lymph Flow Is Directly Proportional to Hydrostatic Pressure and Inversely to Colloid Osmotic Pressure ✚ Hypotension Decreases Lymphatic Flow
Lymphatic Of Limbs	<ul style="list-style-type: none"> ✚ UPPER LIMBS drain into Axillary, infraclavicular, and Infra-pectoral nodes. ✚ LOWER LIMBS drain into Superficial Inguinal (Vertical group) & popliteal nodes. ✚ Big toe drains into a Vertical group of superficial nodes. ✚ Infected nail bed of little finger drains into Supratrochlear lymph nodes. ✚ Index finger drains into Infraclavicular Lymph nodes. ✚ Epitrochlear nodes enlarge in Syphilis. ✚ Medial side of the elbow drains into a Medial group of axillary nodes. ✚ 1st pulp space = Epitrochlear nodes ✚ Popliteal Nodes drain Lateral Foot area. <p><u>Levels Of Axillary Lymph Nodes</u></p> <ul style="list-style-type: none"> ○ There are 5 groups: Anterior (Pectoral) Posterior (Subscapular), Central, apical, and lateral Humeral). ○ Defined according to surgeon's approach to axillary nodes during dissection using Pectoralis Minor as a landmark and divided into three groups as follows: <ul style="list-style-type: none"> ✚ Level 1: Lateral to border of Pectoralis Minor i.e., anterior, posterior, and lateral group. ✚ Level 2: Under Pectoralis minor i.e., Central group ✚ Level 3: Medial to Pectoralis minor muscle i.e., Apical & infraclavicular nodes
Breast	<p><u>QUADRANTS:</u></p> <ul style="list-style-type: none"> ○ Medial and Lateral. There are 4 quadrants: ✚ Superolateral (Upper Outer), Superomedial (Upper Inner) ✚ Inferolateral (Lower Outer), Inferomedial (lower inner) ✚ 70% of cancers of the breast involve the Upper Outer/Superolateral group.

	<p>Pathway Of Axillary Lymph Drainage:</p> <ul style="list-style-type: none"> ○ Anterior and Posterior Nodes ✚ 75% of Lymph of breast drains into the Anterior group (Pectoral group). ✚ Upper Lateral drains into: Ant Axillary/Pectoral mainly ✚ Lower lateral into Ant axillary, Subdiaphragmatic & internal mammary nodes ✚ Medial Quadrant drains into internal mammary / internal thoracic nodes. ✚ Inferomedial quadrant drains into subdiaphragmatic/inferior phrenic nodes. ✚ Nipple drains into Ant Axillary nodes. ✚ Tail of breast drains into Posterior Axillary/Scapular Nodes. ✚ Sentinel lymph node is the 1st node in which cancer drains. ✚ Biopsy of sentinel nodes helps in establishing prognosis of carcinoma. ✚ Axillary lymph node biopsy helps in assessing: Bilateral disease > prognosis regarding breast carcinoma
HEAD & NECK	
Levels Of Neck Lymph Nodes	<ul style="list-style-type: none"> ❖ Level I: Submental (Ia) + Submandibular (Ib) ❖ Level II: Upper Jugular, Level III: Middle Jugular, Level IV: Lower Jugular ❖ Level V: Posterior Triangle Group (Spinal Accessory Grp) ❖ Level VI: Pre-Laryngeal, Pre and Para Tracheal. Level VII: Upper Mediastinal.
Scalp Drainage	<ul style="list-style-type: none"> ❖ Central Scalp: No Lymph Nodes ❖ Anterior Scalp: Submandibular Nodes. ❖ Posterior Scalp: Occipital Nodes ❖ Lateral Scalp: Superficial Parotids L. N
Lips	<ul style="list-style-type: none"> ❖ Upper Lips: Submandibular and pre auricular nodes ❖ Lower lips: Medial part into Submental, Lateral part into Submandibular.
Tongue	<ul style="list-style-type: none"> ❖ Tip: Submental nodes ❖ Anterior 2/3rd (Lateral surface): Ipsilateral Submandibular node ❖ Anterior 2/3rd centrally: Submandibular nodes of both sides ❖ Posterior 1/3rd: Jugulo-Omohyoid nodes. ❖ Final lymph drainage of tongue: Deep Cervical Nodes
Nose, Palate, Pharynx, Larynx & Palatine Tonsils	<ul style="list-style-type: none"> ❖ Nose: anterior nose into Submandibular, Posterior into Retropharyngeal. ❖ Finally drain into Deep cervical nodes ❖ Nasopharynx: drains into Retropharyngeal nodes ❖ Soft & hard palate: Retropharyngeal & deep cervical nodes ❖ Supraglottic Larynx: upper deep cervical, Infraglottic: Lower deep cervical ❖ Palatine Tonsils: Jugulo-digastric lymph nodes.
Trachea, Thymus, Thyroid, parathyroid and parotid gland	<ul style="list-style-type: none"> ❖ Trachea: Pretracheal, para tracheal & Deep cervical nodes ❖ Thymus: Para sternal + tracheobronchial lymph nodes ❖ Thyroid: Deep Cervical nodes ❖ Parathyroid: Deep cervical nodes ❖ Parotid Gland: Superficial Parotid (90%) and deep Parotid Nodes.
Face Lymph drainage	<ul style="list-style-type: none"> ❖ Forehead + anterior Face: Submandibular nodes mainly ❖ Lateral Face + Lateral eye lids: parotid nodes ❖ Lower lip & Chin: Submental nodes
Deep Cervical lymph nodes	<ul style="list-style-type: none"> ❖ Present around internal jugular vein and drain all lymph from head & neck. ❖ Outer circle: made of superficial nodes from Chin to occiput. ❖ Inner Circle: surrounding the Upper airway & GIT.
GIT & ACCESSORY GIT ORGANS	
All lymph of GIT is drained into Cisterna Chyli, Thoracic duct & then finally into Left Subclavian vein.	
Esophagus	<ul style="list-style-type: none"> ○ Cervical Esophagus drains into = Deep cervical nodes ○ Thoracic Esophagus drains into = Posterior Mediastinal nodes ○ Abdominal Esophagus drains into = Preaortic & celiac nodes
Stomach Duodenum Jejunum	<ul style="list-style-type: none"> ○ Stomach: Celiac Lymph nodes ○ Duodenum: Celiac + Superior Mesenteric Lymph nodes ○ Jejunum + ileum: Superior Mesenteric Lymph nodes

Caecum & Appendix, Colon	<ul style="list-style-type: none"> ○ Caecum & Appendix: Lymph along ileocolic artery ○ Colon: Superior & Inferior mesenteric lymph nodes
Rectum + Anal canal	<ul style="list-style-type: none"> ○ Rectum: Upper part: pre rectal + epiploic to pre-aortic nodes ○ Lower rectum: Internal iliac nodes. ○ Upper anal Canal: Internal iliac nodes ○ Lower anal canal: Superficial inguinal Lymph node ○ Verge of anal canal – superficial inguinal nodes.
Liver Gallbladder Spleen Pancreas	<ul style="list-style-type: none"> ○ Liver & Gallbladder: Hepatic nodes at porta hepatis ○ Spleen: Celiac nodes ○ Pancreas: Upper Head: Celiac nodes. ○ Lower head & Uncinate: Mesenteric nodes. ○ Neck, Body, Tail: Pancreatico-splenic Lymph nodes.
GENITOURINARY SYSTEM	
Kidneys Adrenal glands Testes & Ovaries	<ul style="list-style-type: none"> ○ Kidneys + Adrenal glands, Tests + Ovaries. ○ All these drain into: ○ Para-aortic nodes at L2/lumbar nodes/ aorto-caval nodes.
Ureters	<ul style="list-style-type: none"> ○ Abdominal Ureter: Para-aortic at L2 ○ Pelvic Ureter: Common Iliac + internal Iliac Lymph node)
Bladder	<ul style="list-style-type: none"> ○ Bladder: External Iliac + internal Iliac Lymph node > internal Iliac Lymph nodes.

LYMPHATICS OF REPRODUCTIVE SYSTEM	
MALE	<ul style="list-style-type: none"> ○ Testis, Epididymis & Vas deferens: Para-aortic at L2 ○ Prostate: Internal Iliac Lymph node ○ Seminal Vesicles: internal iliac > external iliac Lymph node ○ Scrotum & Skin of Penis/ skin of glans penis: both into Superficial inguinal Lymph node ○ Glans penis: Deep Inguinal Lymph node
FEMALE	<ul style="list-style-type: none"> ○ Ovary, fallopian tube, fundus of Uterus: Follow the ovarian artery to the Para-aortic Lymph node. ○ Junction of Fundus & Fallopian Tube: Follow round ligament of uterus to superficial inguinal L.Ns ○ Body of Uterus, Cervix, Upper Vagina: Lymphatics Follow the uterine vessels to the internal iliac Lymph node. They Follow the broad ligament to the external iliac Lymph node ○ In short: ○ Body of Uterus: External iliac Lymph nodes & Para-aortic. ○ Fundus: Para-aortic & Superficial inguinal Lymph nodes. ○ CERVIX: Laterally: external Iliac, Postero-laterally: Internal Iliac Lymph node. Posteriorly: Sacral nodes. <p><u>VAGINA:</u></p> <ul style="list-style-type: none"> ○ Upper vagina: External & Internal iliac Lymph nodes ○ Middle vagina: Internal Iliac Lymph nodes ○ Lower Vagina: Superficial Inguinal Lymph nodes
INGUINAL LYMPH NODES (Favourite Question Of CPSP)	
Two groups: Superficial and Deep Groups	
Deep Inguinal	They Drain Glans Penis, Corpora and Clitoris
Superficial Inguinal Nodes	<p>12 – 20 Nodes in The Proximal Region of Femoral Triangle Below Inguinal Ligament</p> <p>Two Groups: Horizontal and Vertical</p> <p><u>Horizontal Group:</u></p> <p>Medial and Lateral Horizontal Groups</p> <ul style="list-style-type: none"> ○ Medial Horizontal Group: Drains anterior abdominal wall at the level of umbilicus Perineum, Scrotum, Skin of Penis, Distal Anal Canal (also verge of anus), partially Uterus. ○ Lateral horizontal group drains lymph from back below iliac crest. <p><u>Vertical Group</u></p> <ul style="list-style-type: none"> ○ Drains Buttocks, lower limbs (Thigh, Medial Leg) ○ Superficial Inguinal Nodes Drain into Deep Inguinal Nodes That Finally Drain into External Iliac Nodes. <p>Popliteal nodes receive lymph from superficial vessels accompanying the small saphenous vein, deep areas of leg and lateral foot</p>

INFECTIOUS DISEASES

Location	Important Normal Flora / Colonizers
Skin	Staphylococcus epidermidis
Nose	Staph aureus – not normal flora but they are important colonizers in nose
Mouth	Viridians streptococci
Dental plaque	Streptococcus mutans
Gingival crevices	Anaerobes (Bacteroides, fusobacterium, actinomyces)
Throat	Viridians streptococci
Colon	Bacteroides fragilis > E coli
vagina	Lactobacillus (normal flora) while E coli and Group B streptococci are colonizers
Urethra	Not any imp flora here, but S. Epidermidis, E coli, corynebacterium are imp colonizers

Disease	Incubation Period
Chickenpox	14 – 16 days
cholera	0.5 hours – 4 days
Diphtheria	2 – 6 days
Gas gangrene	1 – 5 days
Gonorrhoea	3 – 5 days
Hepatitis A	2 weeks – 2 months
Hepatitis B	6 weeks – 6 months (longest incubation period)
Hepatitis C	2 weeks – 6 months
Herpes simplex	1 – 3 days
Measles	10 – 12 days
Mumps	14 – 21 days
Influenza	1 – 3 days
Plague	2 – 6 days
Polio	7 – 14 days
Rabies	2 weeks – 2 months or even 1 year
Syphilis	10 days – 3 months
Tetanus	3 days – 5 weeks
Pertussis	5 days – 3 weeks
Tuberculosis	2 – 10 weeks
Meningitis (bacterial)	1 – 7 days
Staphylococcus food poisoning	1 – 6 hours
Salmonella food poisoning	12 – 72 hours
Pin worm	2 – 6 weeks
HIV/AIDS	HIV: 1 – 6 weeks (average 3 weeks), AIDS: 1 – 10 Years
Infectious mononucleosis	2 – 6 weeks
Leprosy	3 months – 20+ years. Slowest growing microorganism
Malaria	12 – 21 days
Dengue	3 – 10 days
COVID-19	2 – 14 days
Common cold	1 – 2 days
Adenoviruses	5 – 7 days

Arthropod	Disease (Type of Pathogen)
Mosquito	Malaria (protozoan), dengue, viral encephalitis, yellow fever, filariasis
Flea	Plague (rat flea) , endemic typhus (rickettsia)
Body louse	Epidemic typhus, tularaemia, relapsing fever
Tick	Rocky mountain spotted fever (rickettsia), Lyme disease (ixodes tick, borrelia bacterium)
Mite	Scabies (Sarcoptes scabiei)
Sand fly	Leishmaniasis (kala azar)
Tsetse fly	African sleeping sickness (Trypanosoma brucei)
Deer fly, horse fly	Tularaemia
Kissing bug (reduviid bug)	Chagas disease
Black fly (mango fly)	River blindness (Onchocera volvulus)

DIARRHEA

Diarrhea is the passage of ≥ 3 loose (unformed) stools per day, or more frequently than normal bowel habits.

Types	<u>Based on duration of illness</u> <ul style="list-style-type: none">○ Acute Diarrhea : less than 2 weeks○ Persistent Diarrhea: more than 2 wks.○ Chronic Diarrhea : more than 4 weeks <u>Based on Osmotic gap</u> <ul style="list-style-type: none">○ Secretory diarrhea : stool Vol > 1L/day , fasting has no effect. May be caused by bacterial toxins or laxatives or excessive bile salts.○ Osmotic diarrhea : Fasting stops diarrhea e.g Lactose intolerance○ Osmotic Gap of < 50 in Secretory diarrhea whereas > 100 in Osmotic diarrhea	
Etiologies	Non-inflammatory (watery diarrhea) Increased secretions, typically mild watery diarrhea <u>Common Etiologies:</u> <ul style="list-style-type: none">🚩 Viruses – Rota virus, Norovirus, adenovirus, CMV🚩 Bacteria: Enterotoxigenic E Coli, C Perfringens🚩 S aureus, Bacillus cereus, vibrio cholera🚩 Parasites: Giardia, cryptosporidium (in AIDS)	Inflammatory (severe bloody diarrhea) Invasive or toxin producing pathogens Mucosal damage and tissue destruction <ul style="list-style-type: none">🚩 Bacteria: Shigella, Salmonella, Enterohemorrhagic🚩 E coli (Shiga toxin), Enteroinvasive E coli, Yersinia, Clostridium difficile🚩 Parasites: Entamoeba histolytica
Travellers diarrhea	<ul style="list-style-type: none">➤ Caused by enterotoxigenic E. Coli (ETEC) mostly.➤ 1st line drug : Bismuth subsalicylate➤ 2nd line drugs: Loperamide & Diphenoxylate (prefer Loperamide)➤ 3rd Line drug : if resistant to above medications; Use Norfloxacin/Ciprofloxacin➤ So, treatment of Resistant Traveller diarrhea or Antibiotics to be preferred is Ciprofloxacin > Norfloxacin➤ If resistant to above all medications: Use Macrolides	
Complications	dehydration & shock, acute renal failure, Electrolyte imbalances, sepsis & DIC	

DEHYDRATION

Severe dehydration	<p><u>2 of these signs:</u> lethargic/unconscious, sunken eyes, skin pinch goes back very slowly, poorly drinks or unable to drink</p> <p><u>Management:</u></p> <ul style="list-style-type: none">○ Give fluid for severe dehydration (Plan C) as given below○ If child has other severe disease, refer urgently to hospital with mother giving oral ORS sips on the way○ If child > 2 years old and cholera is endemic, give antibiotic (macrolides) for cholera <p><u>PLAN C :</u></p> <ul style="list-style-type: none">❖ For Resuscitation, Give IV isotonic crystalloid fluid 20 mL/kg over 10 to 15 minutes. Repeat if necessary.❖ Monitor pulse, Urine output, capillary refill time and mental status❖ After resuscitation, 100 mL/kg fluid is given in 3 hours if child age > 1 year while in 6 hours if age < 1 year❖ Asses the patient every 3 hours and treat according to plan C or shift to plan B <table><tr><th>Age</th><th>Give first 30 mL/kg (out of total 100 ml/kg) fluid</th><th>Give rest of 70 mL/kg fluid</th></tr><tr><td>< 1 year</td><td>In 1 hour</td><td>In 5 hours</td></tr><tr><td>> 1 year</td><td>In 30 minutes</td><td>In 2.5 hours</td></tr></table>	Age	Give first 30 mL/kg (out of total 100 ml/kg) fluid	Give rest of 70 mL/kg fluid	< 1 year	In 1 hour	In 5 hours	> 1 year	In 30 minutes	In 2.5 hours			
Age	Give first 30 mL/kg (out of total 100 ml/kg) fluid	Give rest of 70 mL/kg fluid											
< 1 year	In 1 hour	In 5 hours											
> 1 year	In 30 minutes	In 2.5 hours											
Some dehydration	<ul style="list-style-type: none">○ 2 of these signs: Restless/irritable, sunken eyes, skin pinch goes back slowly, drinks eagerly/thirsty○ Give fluid as per plan B given below along with Zinc supplements and food.○ If child has other serious disease, refer urgently, mother to continue breastfeed + oral ORS sips. Advise mother when to return immediately○ Follow up in 5 days if not improving while in case of confirmed/symptomatic HIV follow up in 2 days <p><u>PLAN B:</u></p> <ul style="list-style-type: none">● Daily fluid requirement: 100ml/kg up to 10kg Wt., 50 ml/kg up to 10-20 kg Wt., for > 20 kg (20 ml/kg)● Deficit replacement: 75 ml/kg ORS to be given over 4 hours● Replace losses: ORS to be given according to diarrheal fluid loss, max of 10 ml/kg fluid per stool. Give Zinc supplements (20mg) for 10 to 14 days												
No dehydration	<ul style="list-style-type: none">○ Not enough signs to classify as some/severe dehydration○ Give fluid (Plan A), food and zinc supplements○ Advise mother when to return immediately○ Follow up in 5 days if not improving while in case of confirmed/symptomatic HIV follow up in 2 days○ Plan A: ORS therapy to prevent dehydration <table><tr><th>Age</th><th>ORS to give after each loose stool</th><th>ORS to provide for use at home</th></tr><tr><td>< 2 years</td><td>50-100 ml</td><td>500 ml/day</td></tr><tr><td>2-10 years</td><td>100-200 ml</td><td>1000 ml/day</td></tr><tr><td>> 10 years</td><td>According to requirement or as much can use</td><td>2000 ml/day</td></tr></table>	Age	ORS to give after each loose stool	ORS to provide for use at home	< 2 years	50-100 ml	500 ml/day	2-10 years	100-200 ml	1000 ml/day	> 10 years	According to requirement or as much can use	2000 ml/day
Age	ORS to give after each loose stool	ORS to provide for use at home											
< 2 years	50-100 ml	500 ml/day											
2-10 years	100-200 ml	1000 ml/day											
> 10 years	According to requirement or as much can use	2000 ml/day											

PNEUMONIA					
Definition	Acute Inflammation of the lung Parenchyma is called Pneumonia				
Classification	<p>May be classified as Lobar pneumonia or Bronchopneumonia.</p> <table> <tr> <td>Typical pneumonia</td><td> <p>Rapid onset, S pneumonia is the most common cause, others are H influenza, Moraxella catarrhalis, Staph aureus, pseudomonas, anaerobes.</p> <p>Presentation:</p> <ul style="list-style-type: none"> high grade fever with chills, productive cough, mucopurulent sputum, pleuritic chest pain and signs of consolidation; dull percussion note, increased vocal fremitus, bronchial breath sounds, dec chest movements Patchy or lobar infiltrates (opacity) on CXR with leucocytosis </td></tr> <tr> <td>Atypical pneumonia</td><td> <p>Slower onset, organisms involved are either of; mycoplasma pneumonia, legionella, chlamydia, and viruses (adenoviruses, RSV, Influenza)</p> <p>Presentation:</p> <ul style="list-style-type: none"> Fever with dry cough, headache, myalgia, arthralgia, diarrhea Respiratory symptoms like chest pain and productive cough-less prominent Bilateral Patchy non-lobar infiltrates on CXR with WBC count normal/raised </td></tr> </table>	Typical pneumonia	<p>Rapid onset, S pneumonia is the most common cause, others are H influenza, Moraxella catarrhalis, Staph aureus, pseudomonas, anaerobes.</p> <p>Presentation:</p> <ul style="list-style-type: none"> high grade fever with chills, productive cough, mucopurulent sputum, pleuritic chest pain and signs of consolidation; dull percussion note, increased vocal fremitus, bronchial breath sounds, dec chest movements Patchy or lobar infiltrates (opacity) on CXR with leucocytosis 	Atypical pneumonia	<p>Slower onset, organisms involved are either of; mycoplasma pneumonia, legionella, chlamydia, and viruses (adenoviruses, RSV, Influenza)</p> <p>Presentation:</p> <ul style="list-style-type: none"> Fever with dry cough, headache, myalgia, arthralgia, diarrhea Respiratory symptoms like chest pain and productive cough-less prominent Bilateral Patchy non-lobar infiltrates on CXR with WBC count normal/raised
Typical pneumonia	<p>Rapid onset, S pneumonia is the most common cause, others are H influenza, Moraxella catarrhalis, Staph aureus, pseudomonas, anaerobes.</p> <p>Presentation:</p> <ul style="list-style-type: none"> high grade fever with chills, productive cough, mucopurulent sputum, pleuritic chest pain and signs of consolidation; dull percussion note, increased vocal fremitus, bronchial breath sounds, dec chest movements Patchy or lobar infiltrates (opacity) on CXR with leucocytosis 				
Atypical pneumonia	<p>Slower onset, organisms involved are either of; mycoplasma pneumonia, legionella, chlamydia, and viruses (adenoviruses, RSV, Influenza)</p> <p>Presentation:</p> <ul style="list-style-type: none"> Fever with dry cough, headache, myalgia, arthralgia, diarrhea Respiratory symptoms like chest pain and productive cough-less prominent Bilateral Patchy non-lobar infiltrates on CXR with WBC count normal/raised 				
Stages	<p>4 stages of lobar pneumonia are as follows;</p> <ol style="list-style-type: none"> Congestion: occurs in first 24 hrs, red heavy and boggy lungs due to vascular dilatation and alveolar exudate containing bacteria Red hepatization: in 2-3 days red firm liver like lungs and airless. Alveolar exudates contain neutrophils, RBCs, and fibrin Gray hepatization: in 4-6 days, gray, brown firm lungs containing fragmented RBCs and alveolar exudates with neutrophils & fibrin Resolution: > 6 days, normal architecture restored, enzymatic digestion of exudate 				
Types	<ul style="list-style-type: none"> Community Acquired Typical Pneumonia Community Acquired atypical pneumonia Hospital Acq pneumonia (48 hr or more after Hosp admission) Ventilator associated (48 hr or more after ETT intubation) Necrotizing pneumonia Hospital associated Pneumonia/Health care associated : when admitted for >2 days in last 90 days and received IV antibiotics in last 30 days. 				
key Facts (V.IMP)	<ul style="list-style-type: none"> Most common cause of community acquired typical pneumonia is streptococcus pneumonia most common cause of lobar pneumonia is streptococcus pneumonia in 90% cases Atypical pneumonia: organisms don't grow on ordinary culture media, not gram stained, resistant to drugs(e.g penicillin) and atypical presentation with extra pulmonary manifestations Atypical pneumonia causing organisms are mycoplasma, chlamydia, and viruses etc. Necrotizing pneumonia is caused by pseudomonas, staph aureus, klebsiella ventilator associated pneumonia caused by pseudomonas hospital acq pneumonia : staph aureus (nosocomial) pneumonia after viral infection (e.g influenza) : S Pneumonia > staph aureus pneumonia in diabetic and alcoholics : klebsiella pneumonia with rusty sputum strep pneumonia pneumonia with currant jelly sputum: klebsiella (also air-fluid level on CXR) pneumonia in aids patient is plasma cell pneumonia (by Pneumocystis Jirovecii) pneumonia in COPD patient by H influenza and Moraxella catarrhalis pneumonia in cystic fibrosis or burn patient by pseudomonas walking pneumonia caused by mycoplasma air condition related pneumonia - legionella 				

	<ul style="list-style-type: none"> ✚ pneumonia with hyponatremia - legionella also pneumonia in renal transplants ✚ yellow purulent sputum of staph aureus pneumonia ✚ pneumonia plus neurologic symptoms by legionella ✚ green sputum - pseudomonas ✚ influenza causes pneumonia in old, debilitated patients (e.g on wheel chair) with B/L infiltrates
Common causes by Age groups	<ul style="list-style-type: none"> ✓ Neonates: Group B Streptococci > E Coli ✓ Children 1 month to 18 yrs.: Viruses (RSV) > Chlamydia, Streptococcal Pneumonia ✓ Young Adults(till 40 yr.) : Mycoplasma is MCC followed by Chlamydia Pneumonia, S Pneumonia ✓ Adults & Elderly Pts: Strep .Pneumonia is the MCC followed by H infl and Viruses
Diagnosis	<p>Sputum Culture is the most widely used test & gold standard for S pneumonia</p> <p>Serology for viruses and other atypical organisms. Neutrophilic leucocytosis with raised CRP</p>
Treatment	<p>Fluroquinolones are the preferred choice (Leflox, Moxifloxacin)</p> <p>Macrolides (Erythromycin, Azithromycin can also be used. Others; Cephalosporins e.g Ceftriaxone</p>
Complications	<ul style="list-style-type: none"> ○ Empyema is the MC complication in 65% cases ○ Lung abscess, Para pneumonic effusion ○ Dissemination leads to Meningitis, osteomyelitis etc.

URINARY TRACT INFECTIONS	
Risk Factors	<ul style="list-style-type: none"> ❖ Most common Nosocomial infection is UTI (source are catheters) ❖ Risk factors include; Renal stones, VUR and Urinary tract anomalies ❖ Females have more risk due to short Urethra and Faecal colonization of urethra. ❖ Remember: Staph Aureus is the Most common cause of: Nosocomial and Wound infections, drains + IV catheters + bed sores infections/decubitus ulcer
Causes	<ul style="list-style-type: none"> ❖ E coli is the most common overall cause of UTI (including sexually active individuals) ❖ Staph. Saprophyticus -- 2nd common cause, especially in young sexually active females ❖ Klebsiella is the 3rd common cause of UTI (klebsiella is an opportunistic organism) ❖ Others; Enterococcus, Proteus, Serratia, Pseudomonas (Fruity odour)
Clinical features & sterile pyuria	<ul style="list-style-type: none"> ❖ Upper UTI or Acute Pyelonephritis presents with Fever, Flank pain/ Costovertebral tenderness, Pyuria. Elevated WBCs, haematuria, and WBCs casts in urine. ❖ Lower UTI: Cystitis/Urethritis Present with Urgency, Frequency, Nocturia and burning micturition. Fever & systemic signs are less evident ❖ Sterile Pyuria is the presence of WBCs in urine with negative urine culture ❖ Renal tuberculosis is the most common cause of sterile pyuria ❖ Others causes; Chlamydia and Gonorrhoea or Treated UTI < 2 weeks prior ❖ Inadequately treated UTI also predisposes to sterile pyuria
Investigations	<ul style="list-style-type: none"> ✚ Urine culture is the gold standard ✚ if Fever is there, choose Blood + Urine culture both. ✚ UTI: <ul style="list-style-type: none"> ➤ Presence of a pure growth of > 10⁵ organisms per mL of the fresh mid-stream urine Sample ➤ Increased leukocyte esterase is a marker of WBC ➤ Increase Nitrates is a marker of bacteriuria Asymptomatic bacteriuria warrants treatment in Pregnant women, Infants and In those with urinary tract abnormalities
Management	<ul style="list-style-type: none"> ○ Fluid intake of at least 2 L per day ○ Cranberry juice, Urinary alkalinizing agent such as potassium citrate ○ Uncomplicated lower UTI : Trimethoprim-sulfamethoxazole is the best initial treatment. ○ Second-line choices are Amoxicillin, nitrofurantoin ○ For Complicated: Use IV Antibiotics : Ciprofloxacin, Ceftriaxone / Macrolides.

Vaginal infections	<ul style="list-style-type: none"> ○ Candida : Thick White Cheesy discharge. Treat with Fluconazole. ○ Trichomonas Vaginalis : Strawberry Cervix , Greenish Yellowish discharge. ○ DOC-Metronidazole ○ Gardenella Vaginalis: Thin White discharge with Fishy Odour, Clue cells. ○ DOC- Metronidazole 																
Pelvic inflammatory disease (PID)	<ul style="list-style-type: none"> ○ Presents with Cervical motion and adnexal tenderness with Purulent cervical discharge ○ May also Include Endometritis , Tubo Ovarian abscess and Salpingitis or hydrosalpinx ○ Chlamydia trichomatis is the most common STD & Overall MCC of PID (e.g Salpingitis) ○ PID In IUCD : Actinomyces is a common cause. ○ Tubo- Ovarian abscess : Gonorrhoea is the common cause ○ Remember: Endometritis is diagnosed by presence of Plasma Cells ○ IL-6 is involved in chorioamnionitis 																
Genital lesions	<ul style="list-style-type: none"> ○ Painless Ulcer + Painless Lymph Nodes seen in Syphilis ○ Painful ulcer + painful Lymph Nodes in Herpes Simplex infection ○ Painless beefy red Ulcer that bleeds is Granuloma inguinale caused by klebsiella donovani ○ Painless Ulcer + Painful nodes : Lymphogranuloma Venerum (C Trichomatis L1-L3) ○ Gonorrhoea presents with non-ulcer genital lesion 																
TORCH infections	<table> <tr> <th>Organism</th><th>Findings</th></tr> <tr> <td>Toxoplasma Gondi</td><td>chorioretinitis, hydrocephalus , intra cranial calcifications</td></tr> <tr> <td>Rubella</td><td>Most common is deafness > cataract, PDA, and cardiac malformations. > 7 weeks -- deafness, < 7 weeks -- cataract 3-8 weeks -- cardiac defects</td></tr> <tr> <td>Cytomegalo virus (CMV)</td><td>hearing loss , paraventricular calcifications , chorioretinitis</td></tr> <tr> <td>Herpes simplex 2 & HIV</td><td>HSV-2 → meningo-encephalitis HIV - diarrhea and recurrent infections</td></tr> <tr> <td>Syphilis</td><td>still birth, congenital syphilis (Saber shins, mulberry molars, Hutchinson teeth , rhagades, depressed nasal bridge)</td></tr> <tr> <td>Parvo virus</td><td>hydrops fetalis</td></tr> <tr> <td>NOTE</td><td>Features common to all torch infections are: Hepatomegaly, jaundice, IUGR, low platelets TORCH infections do NOT cause pneumonia</td></tr> </table>	Organism	Findings	Toxoplasma Gondi	chorioretinitis, hydrocephalus , intra cranial calcifications	Rubella	Most common is deafness > cataract, PDA, and cardiac malformations. > 7 weeks -- deafness, < 7 weeks -- cataract 3-8 weeks -- cardiac defects	Cytomegalo virus (CMV)	hearing loss , paraventricular calcifications , chorioretinitis	Herpes simplex 2 & HIV	HSV-2 → meningo-encephalitis HIV - diarrhea and recurrent infections	Syphilis	still birth, congenital syphilis (Saber shins, mulberry molars, Hutchinson teeth , rhagades, depressed nasal bridge)	Parvo virus	hydrops fetalis	NOTE	Features common to all torch infections are: Hepatomegaly, jaundice, IUGR, low platelets TORCH infections do NOT cause pneumonia
Organism	Findings																
Toxoplasma Gondi	chorioretinitis, hydrocephalus , intra cranial calcifications																
Rubella	Most common is deafness > cataract, PDA, and cardiac malformations. > 7 weeks -- deafness, < 7 weeks -- cataract 3-8 weeks -- cardiac defects																
Cytomegalo virus (CMV)	hearing loss , paraventricular calcifications , chorioretinitis																
Herpes simplex 2 & HIV	HSV-2 → meningo-encephalitis HIV - diarrhea and recurrent infections																
Syphilis	still birth, congenital syphilis (Saber shins, mulberry molars, Hutchinson teeth , rhagades, depressed nasal bridge)																
Parvo virus	hydrops fetalis																
NOTE	Features common to all torch infections are: Hepatomegaly, jaundice, IUGR, low platelets TORCH infections do NOT cause pneumonia																

MENINGITIS

Definition	Inflammation of the meninges surrounding the brain
Causes	<p>May be caused by Bacteria (common cause), viruses or fungi as well</p> <p>Organisms in age groups:</p> <ul style="list-style-type: none"> ○ Neonates : Grp B streptococcus > E Coli > Listeria ○ Children + Young + Adults + Elderly : (6 months age to 65 years +) ○ Strep. Pneumonia (most common) > Neisseria Meningitides (2nd common) ○ Other causes are H Influenza , viruses (entero & echo viruses, herpes) and Listeria ● S Pneumonia is the MCC of Septic Meningitis. ● In HIV – Cryptococcus neoformans fungal causes meningitis. ● HSV- 1 may cause Encephalitis (Temporal Lobe) – MCC of Sporadic Encephalitis ● Infection outside epidemic area is called Sporadic (e.g yellow fever) ● HSV-2 causes Meningitis. ● Listeria causes meningitis in extreme of ages (neonates + elderly 65+) but not the MCC ● H Influenza meningitis risk has reduced due to Conjugated Polysaccharide Vaccine ● Grp B Strept infection dec due to screening of mothers at 3rd trimester (35-37th weeks)
Features	<ul style="list-style-type: none"> ● Fever, Headache & Vomiting (raised ICP) with Nuchal Rigidity (pathognomonic). ● +ve Kerning sign (leg Extension causes Pain) ● Brudzinski sign (Neck flexion causes Knee flexion), ● Bulging anterior fontanelle in infants.
Diagnosis	CSF examination & culture carries prime importance. Findings are given below.

	Blood culture, ESR, CRP, CT brain may be useful.			
	Type	Cell count	Glucose	Protein
	Bacterial meningitis	>1000-2000 cells/mcL Mainly Neutrophils	< 45 or 40 mg/dL	raised >250 mg/dL
	Tb meningitis	100-500 cells/mcL Predominantly Monocytes or lymphocytes	< 45 mg/dL	Raised 100-500 mg/dL
	Viral meningitis	<2000 cells/mcL Mainly lymphocytes	Normal	raised < 150 mg/dL
	Fungal meningitis	100-500 cells/mcL Mainly lymphocytes	Low to normal	Normal to raised
	Remember: <ul style="list-style-type: none"> • Normal Glucose in CSF : 60% of blood glucose or 2 / 3rd . 50 – 80 mg/dl • Normal Protein in CSF : 20-40 mg/dl • Normal CSF is Clear and Colourless with Opening pressure of 6-20 cm H2O. • Blood-stained CSF in Subarachnoid hemorrhage • Turbid CSF in : Acute Bacterial or acute Pyogenic meningitis • Opalescent > Straw colored in Tb meningitis (Cobweb or fibrin coagulum formation) • Clear CSF in Viral & Fungal infection 			
Management	Empirical Therapy <ul style="list-style-type: none"> • IV Ceftriaxone + Vancomycin. • Penicillin G is DOC for N. Meningitidis. Ceftriaxone is overall ,preferred drug for meningitis • Add Ampicillin for listeria infection 			
Complications	<ul style="list-style-type: none"> • Tuberculous meningitis presents with complications mostly i.e Cranial Nerve Palsies , Hydrocephalus, and coma etc. • Most common Operatable Complication is Hydrocephalus • Most Common Sequel is Cranial Nerve 8 palsy (Deafness / Hearing Loss) 			

Brain Abscess

- 📌 **most common site is Frontal > Temporal Lobe**
- 📌 Single lesion arises from Dental or ear infections, whereas multiple lesions from Bacteraemia.
- 📌 Staph Aureus is MCC of brain abscess Viridians Spp in case of dental infection may also cause
- 📌 Nocardia may cause Lung infection + brain abscesses.
- 📌 On CT Brain, single ring enhancing lesion (in frontal lobe mostly) indicates brain abscess

OSTEOMYELITIS	
Definition	<ul style="list-style-type: none"> ○ inflammation of the bone and bone marrow
Causes	<ul style="list-style-type: none"> ○ Staph Aureus: most common cause Overall , assume if no other available source. ○ Sexually active : Neisseria gonorrhoea (rare), septic arthritis more Common) ○ In Sickle cell disease : Salmonella is the main cause ○ Prosthetic joint replacement : Staph Epidermidis ○ Vertebral involvement : Potts disease (Tb) ○ Cat and dog bites : Pasteurella Multocida ○ IV drug abusers : Staph aureus > Pseudomonas and candida.
Route & Findings	<ul style="list-style-type: none"> ○ Spread can occur by local extension, direct implantation and hematogenous Spread ○ Haematogenous is the most common route ○ Acute Osteomyelitis usually begins at Metaphysis ○ Sequestrum is a macroscopic piece of dead bone ○ Involucrum is the new bone formed around an area of Osteomyelitis in response to periosteal stimulation ○ Sub-acute Osteomyelitis: It is a distinct form of in which Brodie abscess may form ○ Brodie's Abscess = Pyogenic Osteomyelitis
Diagnosis	<ul style="list-style-type: none"> ○ Elevated ESR and CRP are less sensitive ○ MRI – Best investigation. Blood culture can be diagnostic.
Management	<ul style="list-style-type: none"> ○ IV antibiotics : cloxacillin/Nafcillin, Ceftriaxone/Ciprofloxacin and gentamycin for 02 weeks then shifted to oral medications

Amoebic liver abscess	<ul style="list-style-type: none"> ○ Presents with Swinging Fever , anorexia , weight Loss, Tender Hepatomegaly. ○ Serology is diagnostic for amoebic Liver abscess. ○ If to do rectal biopsy for amoebic abscess, look for PSA +Ve. ○ Treatment with Metronidazole 800 mg 1 × TDS for 10 days
Pyogenic liver abscess	<ul style="list-style-type: none"> ○ High grade fever with rigors and chills and Pain in Hypochondrium region ○ CT scan is diagnostic. USG can also be done. ○ Most common cause is Ascending Cholangitis and E coli is involved frequently. ○ CT or USG guided drainage is the preferred treatment modality. ○ Antibiotics Ciprofloxacin/gentamycin and metronidazole are given for 4 weeks

PRIONS

- Prion diseases are caused by the conversion of a normal (predominantly α -helical) protein (PrP^c) to a β -pleated form PrP^{Sc}, which is CNS-related tissue Termed CJD) or food contaminated by BSE-infected animal products
- **Resistant to Standard sterilizing Procedures, including standard autoclaving.**
- Features: Spongiform encephalopathy and dementia, ataxia, startle myoclonus, and death.
- Results in Creutzfeldt-Jakob disease – rapidly progressive dementia, typically sporadic
- some familial Bovine spongiform encephalopathy also called mad Cow disease
- Kuru is an acquired prion disease noted in tribal populations practicing human cannibalism

Bugs & Blood Cells

- Bugs inside RBCs = Malaria & Babesia. Rbcs inside bugs = Entamoeba histolytica
- bugs inside macrophages or reticuloendothelial system = Histoplasma, TB and Leishmania spp

VIRAL CONJUNCTIVITIS (PINK EYE)

- A type of follicular conjunctivitis commonly caused by adenovirus- prevalent in Pakistan recently (in Karachi)
- Associated with contagious eye discharge or common cold
- Presents with watery non purulent eye discharge, foreign body sensation in eye, redness, and itching
- No antimicrobial treatment is required as the disease is self-limiting
- Frequent eye washing with cold water is helpful. It is highly contagious, so, avoid contact with the patient

CPSP FAVORITE POINTS + IMPORTANT FACTS

- ✚ Most radiosensitive tumor = Lymphoma > seminoma
- ✚ Vitamins - rich in green vegetables, while Minerals least in tubers + highest in soya beans
- ✚ Bronchopulmonary segment supplied by tertiary bronchus.
- ✚ Renal column / capsule contain interlobar Arteries
- ✚ Glomeruli has interlobular arteries
- ✚ Most aggressive CA is melanoma.
- ✚ Locally Malignant Cancer is BCC > ameloblastoma
- ✚ Median lobe of prostate structurally largest lobe
- ✚ Lateral is the anatomically largest lobe. Peripheral - largest zone
- ✚ CA prostate- peripheral zone and Posterior lobe + Metastasize to Vertebral column and brain by Anterior Intervertebral venous plexus
- ✚ BPH -- median lobe and transitional zone.
- ✚ Congenital SNHL associated with CMV
- ✚ Lichen planus association with Hep C > EBV.
- ✚ External laryngeal nerve is damaged in thyroidectomy
- ✚ Recurrent laryngeal nerve injured in -- tracheotomy.
- ✚ Bronchoscopy -- first seen will be upper lobe of right lung
- ✚ Aspiration most common -- Apical segment of right lower lobe
- ✚ Supine position -- right lower lobe . Lying on right side ➞ right upper lobe
- ✚ Lower airways -- T3-T4
- ✚ PTH regulates Ca and vitamin D levels + Hypertrophy in CRF
- ✚ Breast has --- 15-20 lactiferous tubules + medial side drains into internal thoracic, while upper outer quadrant into Anterior Axillary / pectoral nodes
- ✚ Hemorrhagic Infarcts / red Infarcts ➞ Testes + Intestine + lungs + liver
- ✚ Ischemic Infarcts / pale Infarcts -- heart + spleen + kidneys
- ✚ Becks Triad (Cardiac tamponade)-- Muffled HS, Hypotension and Raised JVP
- ✚ Rustling sound/Pericardial Rub-- Pericarditis
- ✚ Normal individual 70kg (42 liters water). ICF ➞ 28 liters (2/3rd). ECF ➞ 14 liters (1/3rd)
- ✚ ECF further has two parts : Plasma ➞ 3.5 liters. Remaining is Interstitial fluid ➞ 10.5 liters
- ✚ CSF is transcellular fluid
- ✚ Max absorption of water and salts+ Aldosterone independent water absorption + passive sodium absorption -- Jejunum
- ✚ Aldosterone dependent water absorption + Active sodium absorption+ Max efficiency of water absorption --- colon.
- ✚ Duodenum ➞ calcium + iron absorption in Fe+2 (ferrous form in heme)
- ✚ Heme binds with -- hemopexin. Hemoglobin binds with ➞ Haptoglobin
- ✚ Fat necrosis -- pancreas + breast (trauma) + omentum
- ✚ Coagulative (cell outline is preserved) -- seen in kidney + hearts + liver
- ✚ Metastatic calcification -- lungs. Dystrophic -- necrotic tissues
- ✚ Liquefactive necrosis ➞ brain, infections e.g, pus/abscess
- ✚ Amyloidosis (Congo red stain + rectal biopsy) ➞ kidney affected
- ✚ Pulmonary embolism ➞ clinically silent + **sinus tachycardia** + S1Q3T3 + gallium scan
- ✚ Fat embolism ➞ occur after 12 hours + long bones fracture
- ✚ Amniotic fluid embolism ➞ pregnant lady in 3rd trimester
- ✚ Asthma ➞ Decreased FEV1/ FVC ratio -- 0.75
- ✚ Heparin Acts on ➞ activates Antithrombin 3. Heparin Blocks ➞ factor Xa and Thrombin
- ✚ Sarcoidosis (ERYTHEMA NODOSUM) ➞ microscopic (non- caseating granuloma) histology shows epithelioid cells + asteroid bodies + LUNGS most common affected
- ✚ TB (delayed cell mediated type 4 Immunity) ➞ microscopic (caseating granuloma)
- ✚ Histology (epithelioid cells with granuloma) + helper T cells in PPD test + initial for TB X- ray + confirmation AFB by ZN staining + primary Tb (Gohn complex having granuloma with surrounding Lymphatics)

- ✚ Asbestosis → lower lobe of Lungs + bronchogenic CA > mesothelioma (pleural plaques) + FERRUGINOUS BODIES + construction workers + plumbers
- ✚ Silicosis → upper lobe of right + EGG SHELL CALCIFICATION + sandblasting , foundries and mines + Increased risk of TB +
- ✚ Berylliosis → textile industry (cotton). Anthracosis → black lung + due to inhaled carbon
- ✚ Alveolar macrophages or dust cells → fighters in lungs
- ✚ Most common cause of death in SLE is Renal Failure
- ✚ Most common cause of death in Multiple myeloma → Renal failure>>Infection
- ✚ Autoimmune disease effecting single organ → Hashimoto.
- ✚ Hashimoto thyroiditis → Type 4 HSR > Type 2
- ✚ Diagnostic Test for Multiple myeloma → Biopsy > Protein electrophoresis
- ✚ HLA B27 → Ankylosing spondylitis (bamboo spine) + Reiter Syndrome + IBD + psoriatic
- ✚ HLA → used for graft + graft rejection + identical twins have similar HLA
- ✚ Ideal site for HLA typing is buccal smear
- ✚ SLE → sensitive is ANA + specific is anti-Smith > anti ds DNA
- ✚ RA → morning Stiffness + HLA B4
- ✚ Glomerulosa produces → aldosterone, controlled by serum K+
- ✚ Fasciculata (under control of ACTH) → Cortisol (regulates lymphocytes production turn over)
- ✚ Reticularis → androgens
- ✚ Left Gastric vein → Hematemesis in CLD (DOC is telipressin > Octreotide)
- ✚ Bronchial Artery → source of hemoptysis
- ✚ Esophageal vein + paraumbilical veins → dilation in portal HTN
- ✚ Superior rectal vein + left Gastric + paraumbilical veins + esophageal veins → part of portal system
- ✚ Nerve / structure damaged during Appendectomy → iliohypogastric nerve
- ✚ Artery damaged during Appendectomy → Deep Circumflex artery
- ✚ Appendicular artery → terminal branch of ileocolic artery
- ✚ Superficial inguinal ring derived from → externally oblique aponeurosis
- ✚ Deep Inguinal ring → transversalis fascia
- ✚ Facial sheath → formed by transversalis fascia + fascia iliaca
- ✚ Conjoint tendon → formed by aponeurosis of internal oblique and transverses abdominus
- ✚ Prostate drains into → internal iliac L.Ns
- ✚ Cervix → internal iliac + external iliac (prefer internal iliac)
- ✚ Most common source of DVT causing emboli → femoral vein
- ✚ Most common site of DVT → popliteal vein. Most common cause → immobilization
- ✚ Early wound healing + granulation tissue → Type 3 collagen
- ✚ Late wound healing + wound strength → Type 1 collagen
- ✚ Diet deficient in fruits and vegetables → Decreased tensile strength of wound
- ✚ Diet having complete absence of fruits and vegetables → Decreased collagen synthesis.
- ✚ Vitamin C necessary for → hydroxylation of glycine and proline residues
- ✚ Maximum sensory cortex area → Lips. Maximum motor cortex area → dorsum of hand
- ✚ The distance where two stimuli are perceived to be different is Maximum at → back of scapula
- ✚ Extreme flexion of neck- ligament nuchae damaged .Extreme extension- Anterior Longitudinal ligament
- ✚ vertebra held in place by → ant and post longitudinal ligament
- ✚ Vertebra attached to adjacent lamina → Ligamentum flavum
 - Regarding meningitis :
- ✚ Neonate till 6 months → Group B streptococci (S. Agalactiae) > E coli > Listeria
- ✚ 6months till 2 years → Strep pneumoniae > H. Influenza
- ✚ 6 years till 60 years → S pneumoniae > H influenza
- ✚ Above 60 + alcoholics → strep pneumoniae
- ✚ immunocompromised (HIV) / Renal transplant by Cryptococcus meningitis
- ✚ Renin secretion increased by sympathetic stimulation > Hyponatremia > Hypokalemia
- ✚ Aldosterone secretions increased by Hyperkalemia

- ✚ After radiotherapy skin lesions and fibrosis :
acute ➤ desquamation. Chronic ➤ Enderteritis obliterans. Late ➤ lymphoproliferative disorders
- ✚ Vessels of heart ➤ 2 coronary Arteries +1 Atrioventricular +1 Auricular+ 1 Septal
- ✚ Fibroblast has abundant amorphous substance. Fibrocartilage has abundant collagen
- ✚ Pituitary tumor invades / optic chiasma ➤ Bitemporal hemianopia
- ✚ Optic tract lesion ➤ homonymous hemianopia
- ✚ Cytoskeleton ECM to ICM ➤ Integrins
- ✚ Cytoskeleton To ECM ➤ Integrins.
- ✚ ECM to ICM ➤ Intermediate filaments
- ✚ Cells to Cells adhesion ➤ Cadherins
- ✚ Desmosomes ➤ Cytokeratin/Intermediate Filament
- ✚ Transient adhesions ➤ Selectin > E-Cadherins
- ✚ Metastasis is due to Loss of E-Cadherins
- ✚ Leukocyte adhesion ➤ LFA-1
- ✚ WBC attach to endothelium ➤ ICAM
- ✚ Most common premalignant lesion is Leukoplakia. Most lethal premalignant lesion is Erythroplakia
- ✚ most common premalignant condition ➤ Submucosal fibrosis
- ✚ Most lethal premalignant condition - lichen planus
- ✚ premalignant lesion diagnostic ➤ pleomorphism
- ✚ premalignant condition diagnostic ➤ High N/C ratio
- ✚ Malignancy ➤ Metastasis > Invasion > Pleomorphism
- ✚ Premalignant conditions ➤ Lichen planus and Barret esophagus
- ✚ Anterior duodenum perforation ➤ right paracolic gutter > Right iliac fossa > right post subphrenic space
- ✚ Posterior duodenal perforation ➤ lesser sac
- ✚ SYNCHONDROSIS ➤ Primary cartilaginous joint +Hyaline cartilage. Eg Epiphyseal plates of long bones
- ✚ SYMPHYSIS ➤ Secondary cartilaginous joint +Fibrocartilage e.g Intervertebral discs + pubic Symphysis
- ✚ Wrist is condyloid joint. Knee + ankle + Elbow ➤ hinge joint. Hip + shoulder ➤ ball and socket
- ✚ EBV ➤ Nasopharyngeal CA. Oropharyngeal ➤ HPV. Bronchogenic CA ➤ CMV / HPV
- ✚ Primary amenorrhea + webbed neck + short height in a female ➤ turner syndrome (45X0)
- ✚ Absent uterus on scan + well developed breast and normal height ➤ Androgens insensitivity syndrome (46XY)
- ✚ Ambiguous genitalia + 46XX ➤ congenital adrenal Syndrome
- ✚ Blind vagina + absent uterus ➤ testicular feminization /Adrenogenital syndrome
- ✚ Single Palmer crease + mental retarded + low set ears + trisomy 21 ➤ down syndrome
- ✚ Hysterectomy + tubal ligation ➤ ureter damage + uterine artery ligation
- ✚ Oophorectomy (Ovarian fossa) ➤ internal iliac vessels
- ✚ Superficial perineal pouch ➤ rupture of bulbar urethra
- ✚ Deep perineal pouch ➤ rupture of membranous urethra
- ✚ PCT ➤ Maximum reabsorption (67%)
- ✚ HCO₃⁻ ➤ PCT and CD
- ✚ Maximum absorption is of ➤ glucose
- ✚ Drug actively secreted by renal tubules ➤ benzyl penicillin
- ✚ Most Hypotonic urine ➤ DCT. Most Hypertonic ➤ CT
- ✚ Thiazide diuretics ➤ Hypokalemia > Hyperglycaemia > Hyperuricemia > Hypercalcemia
- ✚ Hematuria after sore throat ➤ post streptococcal glomerulonephritis
- ✚ UTI + pyelonephritis ➤ E. Coli
- ✚ Thirst stimulation ➤ angiotensin 2
- ✚ Morphine ➤ Strong mu receptor agonist + Increases bronchial tone +Antidote is naloxone +DOC in acute pancreatitis + Causes bradypnea + miosis
- ✚ Pethidine ➤ Causes fatal excitation when given with MAO Inhibitors
- ✚ Tramadol ➤ Weak mu agonist
- ✚ Nitrates ➤ Weak anaesthetic + strong analgesia + Decreased preload + given in MI for pain relief

- ✚ High first pass effect (Sub- lingual)
- ✚ Highest pulse pressure ➞ Femoral artery> popliteal > Aorta
- ✚ Highest MAP ➞ aorta
- ✚ Highest systolic pressure ➞ Renal artery
- ✚ Highest Oxygen tension ➞ pulmonary artery
- ✚ Adult spinal cord ➞ lower border of L1 or upper border of L2
- ✚ Neonates spinal cord ➞ upper border of L3
- ✚ Tracheostomy in adults ➞ C2-C3 (prefer C2)
- ✚ Tracheostomy in children ➞ C3-C4 (prefer C3)

EMBRYOLOGY:

- ✚ Remnant of gubernaculum ➞ scrotal ligament (male) + Round ligament of uterus and ovarian ligament (females)
 - ✚ Medial umbilical ligament ➞ umbilical arteries
 - ✚ Median umbilical Ligament ➞ urachus
 - ✚ Patent Allantois forms ➞ urachal fistula
 - ✚ Remnant of paramesonephric ducts in males ➞ appendix testes
 - ✚ Limbs buds appear in 4th week
 - ✚ Thymus develops from endoderm of 3rd brachial pouch
 - ✚ Foramen Caecum produces ➞ thyroid
 - ✚ Germ cells arise in yolk sac ➞ 3rd week from EPIBLAST / ECTODERM
 - ✚ Primitive streak (cranially) forms ➞ ectopic anal opening
 - ✚ Urachus forms ➞ median umbilical Ligament
 - ✚ Maxillary artery ➞ derivative of first arch
 - ✚ Tunica vaginalis ➞ remnant of processes vaginalis
 - ✚ Ventral mesogastrium ➞ hepatoduodenal Ligament
 - ✚ Dorsal mesogastrium ➞ gastrocolic ligament
 - ✚ Exo-celomic cavity ➞ derived from hypoblast
 - ✚ Lacrimal glands ➞ developed from surface ECTODERM
 - ✚ Rupture of primitive streak mesoderm cranially will produce ➞ ectopic anal opening
 - ✚ Rupture of primitive streak mesoderm caudally will produce ➞ extrophy of bladder
 - ✚ Notochord is mesodermal derivative while neural tube is ectodermal derivative
-
- Thioridazine ➞ Blocks Dopamine receptors.
 - Cervical Dysplasia caused by ➞ HPV > Multiparty
 - Partial resection of pancreas leads to loss of exocrine function, what finding will present ➞ Absent trypsin in duodenal fluid
 - Hemorrhage due to perforation of lesser curvature of stomach , artery involved ➞ Left gastric artery
 - Pt has painless red purple lesion, oral thrush and diarrhea . what causes the red purple painless skin lesion ➞ HHV-8
 - Main function of cerebellum ➞ Coordination of agonist and antagonist muscles
 - Hepatic adenoma ➞ OCPs + anabolic steroids
 - Angiosarcoma ➞ arsenic + vinyl chloride
 - HCC ➞ aflatoxins
 - Liver malignancy ➞ secondary Metastasis is more common than primary CA
 - Strong antimicrobial effect ➞ OH > H₂O₂ > Superoxide
 - Renal tubular buffer ➞ phosphate. Buffer only in kidney ➞ ammonia
 - Intracellular buffer ➞ proteins
 - RBC buffer ➞ Hemoglobin
 - Narrowest part of urethra ➞ External urethral meatus
 - Shortest and least dilatable ➞ membranous urethra
 - Most dilatable ➞ Prostatic urethra

- Female urethra is prone to infections due to short length
- Landmark for dissection of neck + landmark for neck triangles Scalene anterior
- Landmarks for neck muscle + landmark for examination of neck SCM
- sudden painless vision loss + HTN CRAO. Diabetics CRVO
- Loss of Accommodation in old age Stiffness of lens
- Myasthenia gravis antibodies against presynaptic voltage gated channels
- Diagnostic test ACH receptor antibodies
- Most accurate/confirmatory/gold standard EMG
- Drugs for myasthenia -- initial is neostigmine, while for maintenance therapy is Pyridostigmine .
- Physostigmine crosses BBB immediately and Increase Acetylcholine
- Chancre (painless) Syphilis. Chancroid (painful) Hemophilus Ducrei.
- Vesicles HSV 2. Non ulcer lesions Gonorrhoea
- Warty Lesions of genitalia Chlamydia
- Intraepithelial Lesions of genitalia Paget disease of Vulva (pre-malignant)
- Pre-malignant lesion on face which must be excised Actinic keratosis (caused by UV light)
- Condition having Highest malignant potential Basal cell CA (SCC in situ)
- HCC HBV > HCV. chronicity HCV >> HBV. cirrhosis Alcoholism >> HCV >> HBV
- Blood transfusion most CMV > HCV > HBV
- Lethal transfusion reaction + after transplant CMV
- Most common skin Ca is BCC
- Most common site of BCC is upper lip
- Most common after Basal is Squamous. Most common site of SCC is lower lip
- Lateral Relations of vagina (has abundant elastic tissue) :
- Lateral to upper part of vagina Ureter
- Lateral to middle part of vagina Anterior fibers of Levator Ani
- Lateral to lower part of vagina Urogenital Diaphragm
- Immediate mediator of inflammation+ mediator causing vasoconstriction Histamine
- Delayed mediator Leukotrienes and PG + IL-12
- Fever mediator IL-1 & TNF alpha
- Pain mediator Bradykinin (potent) and PG -E2
- Potent chemotactic factor C5a >> LTB4
- Important role of bradykinin increase vascular permeability
- Chemotactic factor for neutrophils IL-8
- Vimentin connective tissue. Desmin muscles
- Cimetidine (H2 blockers) cytochrome P-450 inhibitor and Increases effects of most of the drugs and decreasing their clearance from liver + Inhibits Sucralfate getting absorbed

SIDE EFFECTS :

- Protamine hypotension
- IUCD bleeding + discharge
- Penicillin bronchospasm
- Chlorpromazine dystonia
- TCAs (analgesic effect in 7-10 days) generalized tonic clonic seizures
- Captopril fetal kidney damage in utero
- Tetracycline teeth abnormality
- Ethambutol Retrobulbar neuritis
- Pyrazinamide Hyperuricemia
- Streptomycin + gentamicin Nephrotoxicity (given with caution)
- Cyclophosphamide hemorrhagic cystitis
- Optic neuritis B12 deficiency
- Peripheral neuritis + high output cardiac failure B1
- Pellagra (3Ds) Niacin B3

- Cheilosis + angular stomatitis ➞ Riboflavin B2
- Part of acetyl CO-A and synthetase ➞ B5
- Transamination for liver- B6 required
- Carboxylation (addition of 1 carbon) ➞ B7
- Methylation + nuclei acid synthesis ➞ B9
- Orofecal route ➞ Hep E > Hep A. Lethal Hepatitis ➞ Hep D
- Pregnancy + fulminant hepatitis ➞ Hep E
- For amoebic abscess ➞ serology
- Pyogenic cyst ➞ CT scan. Hydatid cyst ➞ immunological test / immunoassay.
- Ptosis + Meiosis ➞ Horner syndrome
- Ptosis + Mydriasis ➞ CN 3
- Ptosis + normal pupil ➞ Myasthenia gravis
- reticular fibers ➞ longitudinal appearance under light microscope
- Collagen fibers ➞ lamellar appearance under light microscope
- Forceful expiration ➞ internal intercostal + abdominal muscles (external oblique and rectus abdominus)
- Forceful inspiration ➞ external intercostal
- Laboured breath during stab wound when abdomen is moving more ➞ External oblique

HEMODYNAMICS:

- 🚦 Proliferation of blood stem cells - Growth factor
 - 🚦 Proliferation of RBCs - Erythropoietin
 - 🚦 Reticulocytes count tells --> bone marrow response to anemia
 - 🚦 Coombs test --> autoimmune hemolytic anemia
 - 🚦 Bite cells and Heinz bodies + protection against malaria --> G6pd deficiency (protection against malaria)
 - 🚦 Failure to thrive + family history + target cells --> thalassemia
 - 🚦 most common cause of thrombocytopenia -- ITP
 - 🚦 Most common presentation of thrombocytopenia --- petechial hemorrhage and increased BT
 - 🚦 Most common cause of increased BT -- Aspirin use
 - 🚦 Platelets are produced by megakaryocytes
 - 🚦 Most serious transfusion reaction --> A donor blood given to O recipient
 - 🚦 Howell jolly bodies -- sickle cell anemia
 - 🚦 Helmet cells – DIC. Tear drop cells - myelofibrosis
 - 🚦 Large size platelets + platelets adhesion defects + thrombocytopenia -- Bernard Soulier Syndrome
-
- Osteoporosis ➞ thin and wide trabeculae + long term use of steroid is the cause
 - Osteogenesis ➞ osteoclasts in howship lacunae
 - REGARDING bone ➞ appositional growth
 - Osteoblast ➞ bone making cells + produce ALP
 - Osteoclast ➞ bone resorption
 - Blood supply of spinal cord ➞ Anterior + Posterior spinal arteries > VERTEBRAL Artery
 - Characteristic sign of cerebellar lesion ➞ DYSIDIADOCHOKINESIA
 - characteristic sign of cerebellar disease ➞ NYSTAGMUS
 - MARFAN SYNDROME ➞ Tall + subluxation of lens + dissecting aortic aneurysm
 - OSTEOGENESIS IMPERFECTA ➞ Blue sclera + defective collagen synthesis + bone prone to fracture
 - Virus cause cancer because ➞ it has oncogenes
 - Virus cause cancer by ➞ alterations in proto-oncogene > alteration in protein synthesis
 - Ionizing radiations ➞ cause injury free - radical formation
 - Conduction deafness ➞ defect of external or middle Ear + Weber lateralized to affected Ear + negative Reine test
 - Sensorineural deafness ➞ defect of inner ear or processing centers /CN 8 + Weber lateralized to normal ear + positive Reine test
 - Mixed deafness ➞ both combined + common in old age
 - Man is unable to hear in high frequency sounds ➞ Otosclerosis

- Patient has cast applied now has Decreased muscle mass ➞ Disuse atrophy + Decreased no of actin and myosin + Decreased workload
- Micturition controlled by Pons (stimulatory) + Midbrain (Inhibitory) + processing (cerebral cortex)
- Micturition reflex ➞ sacral segments of spinal cord through pelvic splanchnic nerves S2_S4
- Micturition voluntarily controlled ➞ activating of Pudendal nerve
- Runner in marathon has excessive sweating ➞ Heat exhaustion due to DEHYDRATION
- If Runner in marathon has no sweating ➞ it can be heat stroke
- Athletes at the end of marathon ➞ Increased glucagon and Decreased insulin
- Athletes at rest ➞ more stroke volume and Bradycardia
- Sitting to standing (by gluteus Maximus –inferior gluteal nerve) ➞ Decreased venous return + increased venous tone + increased HR
- Trendelenburg test ➞ if standing on right leg then it's right superior gluteal nerve (gluteus MEDIUS)
- Foot drop (neck of fibula) ➞ CPN (DORSIFLEXION + EVERSIONS IS MAIN ROLE)
- Wrist drop ➞ radial nerve (LOST SENSATIONS ON DORSUM OF HAND + INABILITY TO OPEN HAND AFTER CLOSING)
- Claw hand ➞ ulnar nerve (SUPPLIES MEDIAL 1 AND HALF FINGER and hypothenar Eminence)
- Carpal tunnel Syndrome (thenar atrophy) ➞ median nerve (thenar Eminence + lateral 3 and half fingers)

FRACTURE:

- ✚ Upper limb ➞ clavicle (MIDDLE 2/3RD AND LATERAL THIRD)
 - ✚ Lower limb ➞ tibia (AS ITS MOST SUPERFICIAL)
 - ✚ Overall ➞ clavicle most common injured
 - ✚ Strongest ligament ➞ ILIOFEMORAL LIGAMENT
 - ✚ HIP JOINT INFERIORLY ➞ OBTURATOR EXTERNUS
 - ✚ COMMON SITE OF FRACTURE OF RIB ➞ ANGLE OF RIB
-
- FALSE RIBS ➞ 9th AND 10th. FLOATING RIBS ➞ 11th AND 12th
 - Vertebrae ➞ 33. Spinal nerves ➞ 31 pairs
 - Spinal cord is suspended in dura mater by denticulate ligament
 - Pia matter continues with sulci and fissures of brain
 - Cauda equina ➞ L1-L5 anterior + posterior spinal nerve roots
 - RETE EDGES ➞ Squamous cell CA > VERRUCOUS CA
 - Dysplasia ➞ loss of polarity
 - Metaplasia ➞ change in one normal epithelium with another normal epithelium
 - Anterior to right kidney ➞ liver
 - Anterior to hilum of right kidney ➞ 2nd part of duodenum
 - Whenever there is Decreased po2 ➞ Hypoxic hypoxia .
 - Drug absorption ➞ depends on lipid solubility
 - Substances which can cross ➞ largely hydrophobic but soluble in aqueous solution
 - Highest Aqueous diffusion ➞ digoxin (it increases intracellular Ca ions)
 - cAMP ➞ TSH. CGMP ➞ ANP, BNP, NO
 - Phospholipase G- protein coupled receptors ➞ IP3 and Increases Ca ions
 - Blood loss ➞ normocytic normochromic anemia
 - Blood loss and then GFR is Decreased due to ➞ Decreased atrial blood flow
 - Sertoli cells produce mullerian Inhibitory factor + cause of azoospermia
 - Leydig cells secrete testosterone (potent Protein synthesis)
 - Epididymis - Motility starts here
 - Shortest proerthrocytic phase ➞ P. Falciparum (responsible for Cerebral malaria)
 - Longest proerthrocytic phase ➞ P. Malariae
 - Fever with chills ➞ prefer malaria always
 - CD15 and CD 30 cells ➞ Hodgkin lymphoma (nodular Sclerosis is most common + lymphocytic predominant has better prognosis)

- Young age + blast cells + immature lymphocytes ➞ ALL
- Old age + mature lymphocytes ➞ CLL (Philadelphia Chromosome 9,22)
- EBV causes Burkett lymphoma ➞ c-Myc translocation 8,14 and oncogenesis by gene transcription
- Superficial Epigastric Artery ➞ femoral artery
- Inferior Epigastric Artery ➞ external iliac artery
- Structure passing above piriformis fossa ➞ superior gluteal artery
- Gut loops in a child in X ray ➞ pleuro-peritoneal defect / incomplete pleuro-peritoneal membrane
- Tumor of head of pancreas compress ➞ CBD
- Pain in calf relieved after walking ➞ popliteal artery
- Referred Pain of appendicitis ➞ umbilicus
- Referred Pain of diaphragm (primary Muscle of respiration) ➞ neck and shoulder
- Most medial structure in cubital fossa ➞ median nerve
- Epiploic appendages ➞ sigmoid colon
- Abdominal angina ➞ superior mesenteric artery (supplies till middle 3rd of transverse colon)
- Suprarenal gland ➞ Greater splanchnic nerve
- Filling and pain sensation in bladder ➞ sympathetic (all others parasympathetic)
- Right testicular vein ➞ IVC
- Left testicular vein + left suprarenal vein ➞ left renal vein
- Lumbar outflow is ➞ sympathetic (during lumbar sympathectomy L1 should be saved)
- Pulsating abdominal mass ➞ L1-L3
- Shoulder dislocation inferior ➞ axillary nerve + axillary vessels injured
- Shoulder dislocation anterior (COMMONEST) ➞ axillary nerve +Posterior Circumflex artery
- pus in adductor canal compresses ➞ femoral vein
- infectious mononucleosis ➞ EBV (heterophile antibody Test / anti-sheep/Monospot +Ve)
- Alcoholic ➞ increased AST /SGOT + On microscopy Mallory bodies > piecemeal necrosis ...!
- Liver disease ➞ ALT
- Newborn having yellow diaper stained ➞ biliary atresia (drooling of saliva)
- Child having more unconjugated Bilirubin ➞ Gilbert (liver can't process conjugation of Bilirubin)
- Child or adult having conjugated Bilirubin ➞ Dubin - Johnson Syndrome
- After chemotherapy + stones in duct ➞ APOPTOSIS (activation of caspases)
- Moderator band ➞ right Ventricle
- Pectinate muscle ➞ right atrium

LANDMARK DERMATOMES :

- C2 ➞ posterior half of skull
- C3-C5 ➞ phrenic nerve (Main part by C4)
- C6 ➞ thumbs
- T4 ➞ Nipples
- T7 ➞ xiphoid process
- T8 ➞ IVC
- T10 ➞ umbilicus
- L1 ➞ Inguinal Ligament
- L4 ➞ patella
- T3-T4 ➞ lower airways

REFLEXES:

- Ankle reflex ➞ S1- S2 (main S1)
- Knee jerk ➞ L2-L4 (L3)
- Biceps reflex ➞ C5- C6 (C6)
- Triceps reflex ➞ C6-C8
- Cremasteric reflex ➞ L1-L2
- Anal reflex ➞ S3-S4

COMMON STRUCTURES AT VERTEBRAL LEVELS:

- ✚ Hyoid bone ⇨ C3
 - ✚ Common carotid bifurcation ⇨ C4
 - ✚ Trachea bifurcation ⇨ T4-T5
 - ✚ Bronchial artery formation ⇨ T5-T6
 - ✚ Xiphoid process ⇨ T9
 - ✚ Abdominal aorta bifurcation ⇨ L4
 - ✚ IVC ⇨ L5-T8
 - ✚ Esophagus ⇨ T10
 - ✚ Aortic hiatus ⇨ T12
-
- Progression to Symptomatic stage in HIV ⇨ PCR. Follow up ⇨ Cd4 count
 - Muscle arising from femur and stabilizing Knee joint ⇨ vastus lateralis
 - Stabilizing Patella ⇨ vastus medialis
 - DNA virus ⇨ adenovirus
 - Thymic hypoplasia + absent germinal centers + all 3 infections bacterial , viral and fungal ⇨ SCID cause is adenosine deaminase deficiency)
 - Burton A-gamaglobinemia ⇨ most common Cause of pyogenic (bacterial) infection in this
 - Antibodies produced by ⇨ plasma cells. Antibodies produced in spleen
 - Type 1 collagen ⇨ Fibrocartilage + bone + tendons + fascia
 - Type 2 ⇨ elastic and Hyaline cartilage + vitreous body
 - Type 3 ⇨ blood vessels + uterus
 - Type 4 ⇨ Basement membrane + lens
 - HLA B5 ⇨ Behçet's disease
 - Child died of aneurysm ⇨ Kawasaki disease
 - PAN ⇨ Hep B association
 - Temporal Arteritis ⇨ giant cells
 - Wegner granulomatosis ⇨ C-ANCA + glomerulonephritis + nasal pathology
 - Leprosy ⇨ nasal bone deformation (initially nasal scrapings are done)
 - Soldier returning from hilly areas + cyanosis + vision disorder + chronic ⇨ secondary polycythaemia
 - Man at height felt Dyspnea suddenly ⇨ HAPE (height associated Pulmonary edema)
 - Pregnancy → physiological anemia due to dilution + Decreased TLC + increased RBC mass (polycythaemia) + IDA is common + give Ca , Iron (800 mg) and folate by vegetables (neural tube defects) + Premature rupture of membranes causing chorioamnionitis by bacterial vaginosis(IL-6) + dead fetus expulsion with vaginal discharge and abdominal pain (E coli > toxoplasma gondii)
 - Dysplasia ⇨ HPV>IUCD. Metaplasia ⇨ multiparity
 - Lung abscess + hospital acquired infection ⇨ staph aureus
 - Jaw draining abscess ⇨ Actinomyces Israeli
 - Blood ⇨ Hep C. Sexual contact ⇨ Hep B
 - Pain in peptic ulcer + supra renal gland + peritoneal irritation (GIT till duodenojejunal junction) ⇨ greater splanchnic nerves. From duodenum further ⇨ Lesser splanchnic nerves
 - Complication after lymphoma ⇨ HIV. Complication after Sjogren syndrome ⇨ lymphoma
 - complication after CREST ⇨ pulmonary fibrosis
 - Raynaud's phenomenon ⇨ cyanosis if fingers in cold + associated with Scleroderma
 - Heat loss Depends upon ⇨ Core body Temperature (if not present choose Temperature of External environment)
 - Set point Increased than Hypothalamus ⇨ shivering happens and sweating Decreases (vice versa)

- If a person is lying naked heat loss → radiation and conduction
- Marathon running and having excessive sweating → Heat exhaustion > DEHYDRATION
- If a person has no sweating and then collapsed → heat stroke
- Farmer In a sunny day collapsed → Hyponatremia Due to excessive sweating
- Dyspnea on lying down → retrosternal goitre
- Alcohol detoxification → Peroxisomes (they have oxidases too). Drugs detoxification → SER
- Superficial fascia → loose areolar + adipose tissue
- Above transverse Colon → SMA (abdominal angina + wet Gangrene)
- From LATERAL transverse colon to rectum → IMA

Arteries In Rectum :

- Superior rectal Artery → branch of IMA
- Middle rectal Artery (stays in pelvis) → branch of internal iliac artery
- Inferior rectal Artery → branch of internal Pudendal artery

Bicuspid aortic valve → associated with coarctation of Aorta

- ❖ Swelling Anterior to SCM compressing → External jugular vein
- ❖ Source of nitrogen in urea cycle → aspartate and ammonia
- ❖ Phenylketonuria Decreased conversion to → tyrosine
- ❖ In carcinoid Syndrome → 5HIAA Raised (serotonin syndrome / starts from tryptophan)
- ❖ Glans penis and corpora → deep Inguinal lymph nodes (if not present choose Superficial inguinal)
- ❖ Heart works as a syncytium due to → gap junctions
- ❖ SA node → automaticity + generates impulses at a faster rate + prominent pre- potential + slowest potential + heart rate 40-72 + present at Crista terminalis (upper part of sulcus terminalis)
- ❖ Speed of conduction → His-Purkinje → Atria > Ventricles > AV nodes (SLOWEST)
- ❖ HEART RATE 40-60 → CONDUCTION SYSTEM IN AV node
- ❖ HEART RATE 15-40 → conduction system in purkinji fibers (widest diameter that's why fastest)
- ❖ Epithelium of bladder derived from endoderm. Trigone → mesoderm
- ❖ Transitional epithelium of bladder → endoderm + mesoderm
- ❖ Good pasture Syndrome → hemoptysis , hematuria and glomerulonephritis + liner deposits + Type 2 hypersensitivity
- ❖ Vitamin D resistant rickets → Fanconi Syndrome
- ❖ Rickets (children) / Osteomalacia (adults) → vitamin D deficiency (bowing of legs + frontal bossing)
- ❖ Incisive Foramen → Nasopharyngeal nerve
- ❖ Foramen Caecum → nasal emissary veins
- ❖ Foramen spinosum → middle meningeal artery
- ❖ Superior orbital fissure → 3,4,6, ophthalmic vein + V1
- ❖ Foramen Rotundum → maxillary nerve V2. Foramen Ovale → Mandibular nerve V3
- ❖ Foramen magnum → spinal cord. Jugular Foramen → 9, 10 and 11 nerves
- ❖ Bare area of liver limited by → Coronary ligament
- ❖ Connects liver to anterior abdominal wall → Falciform Ligament
- ❖ Connects liver with first part of duodenum → Hepatoduodenal Ligament (is a portion of lesser omentum contains PORTAL TRIAD)
- ❖ Tail of pancreas lies in lienorenal Ligament
- ❖ Femoral artery pulsations → mid-inguinal point
- ❖ Radial artery pulsations → between Brachioradialis and flexor carpi radialis
- ❖ Facial Artery → palpable at the anteroinferior angle of the masseter muscle against the bony surface of the mandible
- ❖ Axillary artery - continuation of subclavian artery
- ❖ Axillary vein → basilic vein + vena comitantes brachial veins (parallel to brachial artery in arm)
- ❖ thoracic ducts drain at the union of left subclavian and left internal jugular → brachiocephalic trunk
- ❖ At standing minimum pressure → superior sagittal sinus

- ❖ Superficial Epigastric Artery branch of ↗ femoral artery
- ❖ Inferior Epigastric Artery branch of ↗ external iliac artery
- ❖ Burns ↗ risk for DIC + Hyperkalemia > Hyponatremia + Decreased albumin causing edema + contracture formation occurs
- ❖ Worst prognostic for sepsis is ↗ DIC .
- ❖ Keloid ↗ occurs in black Africans.
- ❖ Serosanguinous Fluid ↗ Foreign Body
- ❖ Local factor for delayed wound healing ↗ infection .
- ❖ Systemic factor for delayed wound healing ↗ anemia > malnutrition
- ❖ Old age Decreased wound healing ↗ Hormonal and endocrinological changes.
- ❖ Old man fell and fractured his bone and delayed wound healing ↗ Decreased blood supply.
- ❖ Blood supply of head of femur ↗ children (OBTURATOR artery) + Adults (Retinacular artery > Posterior Circumflex artery)
- ❖ Fracture of femur in old age ↗ long term complication is avascular necrosis (watershed areas)
- ❖ In old age high BP only 1 reading + sleep disturbance ↗ isolated Systolic HTN of old age (due it increased vascular Stiffness)
- ❖ Newborn ↗ C- shaped Vertebral column + circular abdominal cavity + liver has 5% of body weight (largest organ) + sample taken from DORSALIS pedis artery > posterior tibial artery
- ❖ Sample taken in shock ↗ Femoral artery
- ❖ Sample taken for ABGs ↗ heparinized arterial sample
- ❖ Edema + apathy + pigmentation ↗ kwashiorkor
- ❖ Most common Secondary cause of HTN ↗ Renal artery stenosis
- ❖ ESRD ↗ increased creatinine
- ❖ Best measure of GFR ↗ inulin clearance
- ❖ Estimation / clinical measurement ↗ creatinine clearance
- ❖ Decision between dialysis and transplant ↗ creatinine clearance
- ❖ Only intracranial branch of facial nerve ↗ nerve to stapedius
- ❖ GVE ↗ smooth muscles and glands
- ❖ SVA ↗ chorda tympani Anterior 2/3rd of tongue
- ❖ Sympathetic Cholinergic only ↗ sweat glands
- ❖ Neurotransmitter released at post-ganglionic endings ↗ acetylcholine
- ❖ Submandibular + submental lymph nodes ↗ lower lip CA
- ❖ Jugulo-digastric lymph nodes ↗ Palatine tonsils
- ❖ Stratified cuboidal epithelium ↗ sweat glands
- ❖ Vagina ↗ more elastic tissue

BRACHIAL PLEXUS :

- ❖ Posterior cord ↗ radial + axillary nerve. Lateral cord ↗ musculocutaneous + median nerve
- ❖ Medial cord ↗ ulnar + median nerve
- ❖ Direct continuation ↗ supra-scapular nerve
- ❖ Forceps delivery ↗ upper trunk of Brachial plexus injury
- ❖ Shoulder delivery ↗ Klumpke's paralysis
- ❖ Erb's palsy ↗ a paralysis of the arm caused by injury to the upper group of the arm's main nerves, specifically the severing of the upper trunk C5–C6 nerves.

DIFFERENTIATING BETWEEN MENINGITIS :

- 🚦 Protein and glucose normal + increased lymphocytes ↗ viral meningitis
- 🚦 Glucose Decreased + increased lymphocytes + Proteins decreased or maybe normal + clear /straw colored ↗ TB meningitis
- 🚦 Glucose Decreased (>40)+ increased Protein + increased Neutrophils +Turbid CSF ↗ bacterial meningitis

- Patent urachus ↗ urine comes out from umbilicus

- Patent Allantois → urachal fistula. Patent vitelline duct → Fecal matter from umbilicus
- Cloacal membrane caudally patent → ectopic anal opening
- Cloacal membrane cranially patent → extrophy of bladder
- Giant cell tumor (soap bubble appearance) → Epiphysis
- Osteosarcoma (Codman triangle sunburst appearance) – metaphysis
- Osteochondroma (most common benign) → metaphysis
- Ewing sarcoma (onion skin) → diaphysis
- Osteblastoma → vertebrae
- Osteoid osteoma → cortex of long bones + has radiolucent osteoid core
- D dimers → sensitive for DVT. FDP → specific for DVT
- Acute endocarditis → staph aureus
- Sub-acute + dental procedures → strep viridians
- Rheumatic heart disease → pansystolic murmur (MS) + given penicillin and gentamicin
- Superior thyroid artery is branch of external carotid
- Inferior thyroid → Thyrocervical trunk
- Thick jelly mucoid sputum (currant jelly sputum) → klebsiella
- Thick jelly sputum after influenza pneumonia → staph aureus
- Farmer lung disease → aspergillosis
- Farmer feet → cutaneous larva migrans
- Histoplasmosis affects → reticuloendothelial system
- Blood - thymus barrier → protects T- lymphocytes from autoimmune destruction
- Pain unrelated to respiration → myocarditis
- Conduction system of heart → sub-endocardium
- Hyaline cartilage → larynx + articular surfaces of Synovial joints
- Elastic cartilage → Ear pinna + nose
- Antibodies against presynaptic Ca channels → Lambert eaten Syndrome
- Blue cell tumor in children + releasing catecholamines + gene Amplification → Neuroblastoma
- Radiation induced Brain malignancy → meningioma
- Overall radiation induced CA → leukaemia
- Absent seizures DOC → Ethosuximide. Generalized tonic clonic → valproic acid
- Liver Decompensation → oxazepam > lorazepam can be used
- Shortest acting → midazolam
- Steroid given for maturation of fetal lungs → betamethasone
- Hyaline disease / disease of Prematurity → Decreased type 2 pneumocytes (Decreased surfactant -- Decreased surface tension -- increased tendency of lung to collapse)
- Lung compliance → provided by surfactant
- First cry → necessary for Pulmonary function
- Commonest Congenital heart anomaly → VSD
- Common Cyanotic anomaly → TOF. Common Cyanotic Anomaly at birth → TGA
- Congenital anomaly in Prematurity + mother living on hilly areas → PDA
- Jaundice After 24 hours → physiological jaundice. Before 24 hours → pathological jaundice
- Erythroblastosis fetalis → if mother is positive then there is no need to worry
- BUT if mother is negative and father is homozygous positive then ALL CHILDREN WILL BE POSITIVE
- Autosomal dominant → 50% children affected + only one parent is affected + co-dominance pattern of inheritability + heterozygotes can cause disease. Examples are → retinoblastoma + HNPCC
- X- linked recessive → Duchene muscular dystrophy (absent dystrophin gene + Positive Gower sign) + familiar occurrence
- Sickle cell anemia → Hemolytic crisis
- knee and hip flexor → SARTORIUS
- Knee flexor and hip extensor → HAMSTRING MUSCLES (major is semitendinosus + others are biceps femoris and semimembranosus)

- Knee extensor and hip flexors ➞ QUADRICEPS MUSCLES (rectus femoris + vastus medialis + vastus lateralis + vastus intermedius)
- Athletes (tennis players) having severe pain + ecchymosis / swelling over ankle ➞ Plantaris tendon rupture + Plantaris muscle involvement
- Lower limb sensation ➞ fasciculus gracilis. Upper limb sensation ➞ fasciculus cuneatus
- Anterior cruciate ligament ➞ prevents backward dislocation of femur on tibia
- Posterior cruciate ligament ➞ prevents forward dislocation of femur
- Popliteus ➞ unlocking of knee + has intra-articular tendon
- Intra-articular injection nerve damage ➞ Sciatic nerve > Superior gluteal nerve
- CALCANEUM is the largest tarsal bone + most commonly fractured bone of foot + makes lateral longitudinal arch
- CALCANEONAVICULAR LIGAMENT ➞ provides support to MEDIAL LONGITUDINAL ARCH (pillar is Talus bone Which has no muscle attachment) + FLATFOOT (if damaged)
- Largest sesamoid bone ➞ PATELLA
- Ideal site of venous grafting ➞ saphenous vein

MICROBIOLOGY:

- Torrential diarrhea and donut shaped crystals ➞ cryptosporidiosis
- Motile Pear-shaped organism + green discharge ➞ Trichomonas
- Motile Pear-shaped organism + greyish discharge ➞ Giardiasis
- Death due to lethal diarrhea ➞ Vibrio cholera
- Death due to food poisoning ➞ Clostridium botulinum
- Dry heat kills by oxidation. Moist heat ➞ coagulation
- Decreased vision + nodules under skin + lives near river ➞ Onchocerca volvulus
- Decreased vision + worms in eye + conjunctivitis ➞ Loa Loa
- Plague caused by Yersinia pestis
- Plague transmitted by Rodent Flea
- Coagulase +ve ➞ Staph aureus
- Catalase +ve ➞ staph epidermis
- Alpha toxins + phospholipase ➞ C. Perfringens
- Fruity smell ➞ Pseudomonas aeruginosa
- Macrocytic anemia ➞ Diphyllbothrium Latum (fish tapeworm)
- 90% of anthrax infection leads to skin lesions
- Nasopharyngeal sinusitis + greyish exudative membrane + enlarged lymph nodes - Corynebacterium
- Pneumonia in HIV by Pneumocystis Jirovecii
- Live vaccine ➞ MMR. Toxoid vaccine ➞ diphtheria + Tetanus
- clear cytoplasm and HALO around it ➞ CYTOCOCCUS NEOFORMANS
- common cause of PID ➞ Chlamydia. PID in case of IUCD ➞ Actinomyces
- Tubo-ovarian abscess ➞ Gonococcus
- Multiple draining abscess + yellow Sulphur granules ➞ Actinomyces Israeli
- Pregnant female + foul smelling discharge + dead fetus delivery premature ➞ Treponema pallidum
- In OT ➞ frequency hand washing (by chlorhexidine and alcohol)
- Floor disinfection in HIV ➞ 1 % hypochlorite Instruments ➞ 2% glutaraldehyde
- Humidity in OT = 55%
- In influenza ➞ vaccine is 60% preventive so choose it for primary prevention
- Primary prevention ➞ before a disease (vaccination or any other prevention)
- Secondary prevention ➞ after a disease vaccination
- Specific protection ➞ against a specified disease (giving vit D to children or giving folate to mothers

CARDIOLOGY :

- ➡ Irregular R-R interval + irregularly irregular pulse ➞ atrial fibrillation

- 🚦 Saw tooth waves → atrial flutter
- 🚦 Difference in BP in both arms + notching if ribs → coarctation of Aorta (post-ductal)
- 🚦 Wide pulse pressure difference + increased EDV + Diastolic murmur → Aortic Regurgitation
- 🚦 During extra systole → Decreased pulse pressure due to Decreased stroke volume
- 🚦 After extra systole → Increased pulse pressure due to increased contractility
- 🚦 Mobitz type 2 → atrial rate greater than ventricular rate
- 🚦 Determinant of Preload → EDV. Determinant of afterload → MAP
- 🚦 Determinant of TPR → Diastolic BP
- 🚦 Atherosclerosis (fatty streak first prominent sign) → Diastolic HTN
- 🚦 First heart sound - isovolumetric contraction (closure of mitral + tricuspid valve) + felt at mitral area
- 🚦 Second heart rate - isovolumetric relaxation (closure of aortic and Pulmonary valve) + felt at left upper sternal border
- 🚦 Third heart sound → rapid ventricular filling + best at apex + normal in children, pregnancy and athletes
- 🚦 Fourth heart sound → non-compliant left Ventricle + best at apex + due to increased atrial pressure
- 🚦 Highest oxygen consumption → isovolumetric contraction
- 🚦 Tall QRS complex → LVH
- 🚦 A-wave of JVP → coincides with PR interval + absent in Atrial fibrillation
- 🚦 Anterior interventricular groove → great cardiac vein + anterior interventricular artery (LAD)
- 🚦 Posterior interventricular groove → middle cardiac vein + posterior interventricular artery (RCA)
- 🚦 RV → most anterior part + Commonly Injured in trauma
- 🚦 Left atrium dilation → compresses esophagus + RLN (Ortner syndrome)
- 🚦 Anterior border of heart → right Ventricle
- 🚦 Diaphragmatic border → left ventricle
- 🚦 Right border of heart → right atrium. Right border on x ray → Right atrium + SVC
- 🚦 Stab Injury at 5th-6th ICS → Right atrium
- 🚦 Pericardium → supplied mainly by pericardiophrenic arteries + phrenic nerve
- 🚦 Epicardium → supplied by Coronary arteries
- 🚦 Apex → LAD (Anterior interventricular artery)
- 🚦 RBB → LCA
- 🚦 inferior wall Mi → RCA > (RMA)
- 🚦 Anterior wall Mi → LAD
- 🚦 Lateral wall MI → LCX (left atrium + left ventricle)
- 🚦 Right and left ventricles → Posterior Descending artery
- 🚦 SA node → RCA mainly

NEUROLOGY :

- Covering of Peripheral Nerve :
- Endoneurium --- individual nerve fiber. Injured in GBS
- perineurium ---- bundle of nerve fibers
- Epineurium --- entire Nerve
- Nodes Ranvier → contains Na⁺ channels.
- marker of astrocytes → GFAP
- Neural tube defects → AFP raised + increase Acetylcholinesterase (confirmatory)
- Arachnoid matter → avascular space
- Blood supply of scalp → External carotid artery (three branches Superficial temporal + Posterior auricular + occipital)
- blood supply of scalp is in dense connective tissue layer > loose areolar layer
- loss of light reflex but intact accommodation reflex → pretectal nucleus (midbrain at the level of superior colliculus)
- Loss of Accommodation reflex → cerebral cortex

- Loss of Accommodation + 3rd CN involvement ➞ Midbrain (due to Edinger Westphal nucleus)
- Corneal reflex lost ➞ Pons lesion
- Right side weakness + double vision on seeing left ➞ MIDBRAIN (involved in movement of eyes + auditory and visual processing)
- Lower face weakness (face deviation)+ contralateral spastic hemiplegia of both upper and lower limb ➞ Internal Capsule (opposite side)
- inhibition of feeding - lateral hypothalamus . inhibition of satiety center- ventromedial hypothalamus
- Sexual center ➞ NUCLEUS ACUMBENS
- cooling + parasympathetic effect ➞ ANTERIOR HYPOTHALAMUS
- Heating + sympathetic effect ➞ POSTERIOR HYPOTHALAMUS
- OVERALL TEMPERATURE CONTROL ➞ ANTERIOR HYPOTHALAMUS
- Astereognosis is inability to recognize objects while eyes closed ➞ associated with lesions of the :
 - DORSAL COLUMN
- FOLIA ➞ CEREBELLUM FOLDS
- HYPERACUSIS ➞ Geniculate ganglion (medial wall of middle Ear)
- Broca aphasia ➞ motor aphasia + non-fluent + area 44 and 45 + inferior frontal gyrus
- Wernicke aphasia ➞ sensory aphasia + fluent + area 22+ superior temporal gyrus
- Global aphasia ➞ both Wernicke and Broca aphasia + arcuate fasciculus
- Anomic aphasia ➞ mild fluent aphasia + failure of word retrieval + angular gyrus
- lesion in DCML ➞ SENSORY ATAXIA + ASTEROGNOSIA
- Reduced motivation and depression ➞ FRONTAL LOBE
- RESTING TREMORS ➞ SUBSTANTIA NIGRA. INTENTIONAL TREMORS ➞ CEREBELLUM
- papez circuit in limbic system connects ➞ Fornix + Mammillary body + Thalamus + Cingulate gyrus
- Fastest fibers ➞ A alpha. Fast pain fibers ➞ A delta
- Slow pain fibers ➞ C fibers
- preganglionic fibers ➞ beta fibers. postganglionic fibers ➞ C fibers
- Type A fibers ➞ pressure. Type B ➞ Hypoxia. Type c ➞ Anaesthesia. Itching ➞ Slow C fibers
- Thirst zone ➞ area postrema and nucleus tractus solitarius
- tractus solitarius ➞ 2nd order neurons and carry taste sensations
- Sleep centre ➞ preoptic nucleus
- Circadian rhythm ➞ suprachiasmatic nucleus
- Chorea (jerky+ quick movements) ➞ caudate nucleus (basal ganglia)
- Athetosis (slow + writhing to) ➞ Globus Pallidus lesion
- hemi-ballismus ➞ Sub-thalamic nucleus lesion
- fusiform gyrus (TEMPORAL LOBE) ➞ FACIAL RECOGNITION (unable to recognize face called prosopagnosia)
- cingulate gyrus (LIMBIC SYSTEM) ➞ EMOTIONS
- Hippocampus ➞ short term memory + recollection in long term memory (long term memory formed by new Protein synthesis)
- large receptive field ➞ PAIN and TEMPERATURE
- Structure close to crus cerebri ➞ substantia nigra
- medial lemniscus formed by decussation of ➞ INTERNAL ARCUATE FIBERS
- In UMN lesion fibers decussate at the level of ➞ PYRAMID
- cerebellum connected to Midbrain by ➞ superior cerebellar peduncle
- Sub-dural hematoma ➞ emissary veins (superior cerebral veins) + common in Alcoholics and shaken babies + crescent shaped
- Epidural hemorrhage ➞ middle meningeal artery (branch of maxillary artery) + LUCID INTERVAL (unconsciousness) + biconvex shaped
- Subarachnoid hemorrhage ➞ rupture of saccular aneurysm + worst headache of life + increased risk for hydrocephalus
- Spinal nerves ➞ mixed nerves (both sensory and motor fibers) + formed in intervertebral Foramina + exit intervertebral Foramina
- spinal ganglia has ➞ pseudo unipolar neurons

- Dysphagia + Dysarthria + analgesia + thermoanaesthesia + ipsilateral hominor Syndrome ➞ lesion of PICA
- Anterior Spinothalamic tracts ➞ pressure and crude touch
- Lateral Spinothalamic tract ➞ pain and Temperature
- Dorsal column ➞ fine touch + pressure + vibrations + proprioception
- abundant at finger pads ➞ Meissner corpuscles for (LIGHT TOUCH)
- Pacinian corpuscle ➞ vibrations and pressure
- rapidly adapting ➞ Pacinian > Meissner
- Ruffini nerve endings ➞ sustained pressure (SLOW ADAPTATION)
- Meissner nerve endings ➞ position + deep touch + secrete serotonin
- Fine, discrete movements of hand carried through Corticospinal tracts
- centre for direct autonomic reflexes ➞ Hypothalamus (only OLFACTION does not relay here)
- autoregulation of cerebral perfusion ➞ primarily by PCO₂
- MCA (upper limbs + aphasia) ➞ Insula and Opercula . ACA (lower limbs + aphasia)
- Tabes Dorsalis ➞ Atonic Bladder
- AICA (face +taste + salivation + lacrimation) ➞ branch of basilar artery
- PICA (hoarseness + gag reflex + dysphagia) ➞ branch of vertebral artery
- proximal muscle flexion ➞ rubrospinal tracts
- Proximal muscle extension ➞ vestibulospinal tracts

COMMUNITY MEDICINE:

- T-test Done to compare 2 categories
- ANOVA test Done to compare 3 categories
- Chi -square done to see if distribution of categorical variables differ from one another + distribution of frequencies + includes 2 x2 Tables
- Specificity excludes true negatives after positive screening. Sensitive includes all positives (true +Ve)
- Positive predictive value ➞ includes true positive after a positive screening test
- negative predictive value ➞ includes persons who had negative screening test and are truly negatives
- Pie chart ➞ different percentages given (famous example of CPSP that 20% postmenopausal females need HRT, 40% don't need HRT and 40% are absolutely normal)
- Regression analysis ➞ estimating relationship of dependent variable with independent variable
- [Famous example of CPSP student seeing changes in temperature changes in patients during surgery over a specific time]
- Data ➞ are individual pieces of factual information recorded and used for the purpose of analysis. It is the raw information from which statistics are created.
 - **CASE CONTROL** : Effect to cause
- E.g => Two groups having lung cancer. Then relating the lung cancer to its cause of risk factor such as smokers and non-smokers (retrospective study)
 - **COHORT STUDY** : cause to effect
- E.g => two groups :
- 1---> CHD and associated risk factor
- 2---> CHD and no risk factor
- E.g=> association of smoking with lung cancer
- **Randomized control trial** ➞ random choosing of groups of individuals of a specific disease
- Eg a Dr operated 20 patients surgically and choose 10 patients among them and seeing it's result after 6 months this is an example of randomized control trial
- **Single blind** ➞ Only Dr knows about the efficacy of drug
- Double blind ➞ Both doctor and Patient don't know about the efficacy of drug
- Mean ➞ adding all No's and dividing it by no of variables
- Mode ➞ most repeated no in a calculation
- Median ➞ making two halves and choosing the middle one
- Standard deviation ➞ Mean and its standing error on both sides of normal distribution curve
- Incidence ➞ Newly diagnosed cases

- Prevalence ⇨ overall total cases
- Cloacal membrane cranially ⇨ ectopic anal opening
- caudally ⇨ extrophy of bladder
- Soybeans ⇨ unsaturated fatty acids
- Vegetable oil ⇨ saturated fatty acid
- Structure damaged during delivery + major support of Pelvic viscera ⇨ Levator Ani (made by pubococcygeus > puborectalis)
- Cutting in mediolateral episiotomy ⇨ Bulbospongiosus
- Main support of uterus ⇨ transverse cervical ligament / cardinal ligament
- Vitamin k deficiency may occur ⇨ after antibiotics
- Vitamin A excess ⇨ scaly dermatitis > jaundice
- Vitamin A deficient ⇨ night blindness (symptom) and conjunctival xerosis (sign)
- VITAMIN E ⇨ antioxidant + deficiency causes muscular dystrophy > Hemolytic anemia
- Glutathione ⇨ strongest antioxidant. Glutathione > Vit E > Vit C > Vit A
- Neutrophils related to bar body + oxidative burst related to antimicrobial Killing + free radicals formation
- Bar body ⇨ 1 is normal in females + scanty in Turner syndrome

REGARDING HB:

- Hb formation starts in pronormoblast / proerythroblast
- Hb starts appearing at intermediate normoblast stage
- Hb maximum rate of synthesis - intermediate and late normoblast
- RBC nuclei disappears in late normoblast (orthochromatic erythroblast)
- Hb becomes max in concentration - reticulocytes > late normoblast

EDEMA:

- Increased hydrostatic pressure ⇨ heart failure
- Increased capillary permeability ⇨ toxins + infections
- Increased interstitial fluid colloid osmotic pressure ⇨ lymphatic blockage
- Decreased plasma proteins / Decreased plasma colloid osmotic pressure ⇨ Nephrotic syndrome + liver failure + protein malnutrition
- Cause of Generalized Edema ⇨ decreased albumin
- Cause of edema In Ascites ⇨ portal hypertension
- Factor preventing edema ⇨ arteriolar constriction
- Burns ⇨ Decreased albumin > increased vascular permeability
- Lymphatic flow Decreased in hemorrhage
- In Diabetes common non-infectious Gangrene is DRY GANGRENE
- But whenever it states diabetic Limb or Diabetic foot it's WET GANGRENE

LAB FINDINGS IN HEMATOLOGY :

- ✓ aPTT raised only -- haemophilia
- ✓ aPTT and BT raised -- vWD
- ✓ aPTT and PT raised -- vit deficiency or liver disease (if doesn't improve by giving vit k)
- ✓ if all 3 raised --- Think for DIC)

COMMONLY TESTED FACTS

- ✚ Acromegaly – Diagnosis: OGTT followed by GH conc.
- ✚ Cushing's – Diagnosis: 24hr urinary free cortisol. Addison --> short synacthen.
- ✚ Rash on buttocks – Dermatitis herpetiformis (coeliac disease related).
- ✚ AF with TIA --> Warfarin. Just TIA's with no AF --> Aspirin
- ✚ Herpes encephalitis --> temporal lobe calcification OR temporoparietal attenuation subacute onset i.e. Several days.
- ✚ Obese woman, papilledema/headache = Benign Intracranial Hypertension.
- ✚ Drug induced pneumonitis by methotrexate or amiodarone.
- ✚ chest discomfort and dysphagia = achalasia.
- ✚ foreign travel, rash/flu like illness = acute HIV
- ✚ Cause of gout --> dec urinary excretion.
- ✚ Bullae on hands and fragile SKIN torn by minor trauma --> porphyria cutanea tarda.
- ✚ Splenectomy - need pneumococcal vaccine AT LEAST 2 weeks pre-op and for life.
- ✚ primary hyperparathyroidism --> high Ca, normal/low PO4, normal/high PTH (in elderly).
- ✚ Middle aged man with KNEE arthritis --> gonococcal sepsis (older people -> Staph).
- ✚ sarcoidosis, erythema nodosum, arthropathy --> Lofgren's syndrome benign, no Rx needed.
- ✚ electrolytes disturbance causing confusion – low/high Na.
- ✚ contraindications lung Surgery --> FEV dec Bp 130/90, Ace inhibitors (if proteinuria analgesic induced headache.
- ✚ 4 cm difference b/w kidneys -> Renal artery stenosis --> Magnetic resonance angiogram.
- ✚ temporal tenderness--> temporal arteritis -> steroids > 90% ischemic neuropathy, 10% retinal art occlusion.
- ✚ severe retro orbital, daily headache, lacrimation --> cluster headache.
- ✚ pemphigus – involves mouth (mucus membranes), pemphigoid – less serious NOT mucosa.
- ✚ diagnosis of polyuria -> water deprivation test, then DDAVP.
- ✚ insulinoma -> 24 hr supervised fasting hypoglycemia.
- ✚ Diabetes Random >7 or if >6 OGTT (75g) -> >11.1 also seen in HCT.
- ✚ causes of villous atrophy: coeliac (lymphocytic infiltrate), Whipple , dec Ig, lymphoma, trop sprue (give tetracycline).
- ✚ diarrhea, bronchospasm, flushing, tricuspid stenosis -> gut carcinoid c liver Mets.
- ✚ hepatitis B with general deterioration -> hepatocellular carcinoma.
- ✚ albumin normal, total protein high -> myeloma (hypercalcemia, electrophoresis).
- ✚ HBsAg positive, HB DNA not detectable --> chronic carrier.
- ✚ Inf MI, artery involved -> Right coronary artery.
- ✚ **Aut dominant conditions:** Achondroplasia, Ehler Danlos, FAP, FAMILIAL hyperchol, Gilberts, Huntington's, Marfans's, NFT I/II, Most porphyria, tuberous sclerosis, vWD, Peutz-Jeghers.
- ✚ X linked: Beck/Duchenne muscular dystrophy, Alport's, Fragile X, G6PD, Hemophilia A/B.
- ✚ Loud S1: MS, hyperdynamic, short PR. Soft S1: immobile MS, MR.
- ✚ Loud S2: hypertension, AS. Fixed split: ASD. Opening snap: MOBILE MS, severe near S2.
- ✚ HOCM/MVP - inc by standing, dec by squatting (inc all others). HOCM inc by Valsalva, decs all others. Sudden death athlete, FH, Rx. Amiodarone, ICD.
- ✚ MVP sudden worsening post MI. Harsh systolic murmur radiates to axilla.
- ✚ Dilated Cardiomyopathy: Bp, thiamine/selenium deficiency, MD, coxsackie/HIV, pregnancy, doxorubicin, infiltration (HCT, sarcoid), tachycardia.
- ✚ Restrictive Cardiomyopathy: scleroderma, amyloid, sarcoid, HCT, glycogen storage, Gaucher, fibrosis, hypereosinophilia Löffler's, carcinoid, malignancy, radiotherapy, toxins.
- ✚ Tumor compressing Respiratory tract --> investigation: flow volume loop.
- ✚ Gullian Barre syndrome: check Vital Capacity.
- ✚ Horner's – sweating lost in upper face only – lesion proximal to common carotid artery.
- ✚ **Internuclear ophthalmoplegia:** medial longitudinal fasciculus - connects CN nucleus 3-4. Ipsilateral adduction palsy, contralateral nystagmus. Aide memoire (TRIES TO YANK THE ipsilateral BAD eye ACROSS THE nose).

- Convergence retraction nystagmus, but convergence reflex is normal. Causes: MS, SLE, Miller fisher, overdose (barb, phenytoin, TCA), Wernicke.
- ✚ Progressive Supranuclear palsy: Steel Richardson. Absent voluntary downward gaze, normal doll's eye . i.e. Oculomotor nuclei intact, supranuclear Pathology .
 - ✚ Parinaud syndrome: dorsal midbrain syndrome, damaged midbrain and superior colliculus: impaired up gaze, lid retraction, convergence preserved. Causes: pineal tumor, stroke, hydrocephalus, MS.
 - ✚ Dementia, gait abnormality, urinary incontinence. Absent papilledema-->Normal pressure hydrocephalus.
 - ✚ acute red eye -> acute closed angle glaucoma >> less common (ant uveitis, scleritis, episcleritis, subconjunctival hemorrhage).
 - ✚ wheals, URTICARIA , drug induced -> aspirin.
 - ✚ sweats and weight gain -> insulinoma.
 - ✚ diagnostic test for asthma -> morning dip in PEFR >20%.
 - ✚ Causes of SIADH : chest/cerebral/pancreas Pathology , porphyria, malignancy, Drugs (carbamazepine, chlorpropamide, clofibrate, antipsychotics, NSAIDs, rifampicin, opiates)
 - ✚ Causes of Diabetes Insipidus: Cranial: tumor, infiltration, trauma Nephrogenic: Lithium, amphotericin, demeclocycline, prolonged hypercalcemia/hyponatremia, FAMILIAL X linked type
 - ✚ bisphosphonates: inhibit osteoclast activity, prevent steroid induced osteoporosis (vitamin D also).
 - ✚ returned from airline flight, TIA-> paradoxical embolus do TOE.
 - ✚ alcoholic, given glucose develops nystagmus -> B1 deficiency (Wernicke's). Confabulation-> Korsakoff.
 - ✚ mono-arthritis with thiazide -> gout (neg birefringence). NO ALLOPURINOL for acute.
 - ✚ painful 3rd nerve palsy -> posterior communicating artery aneurysm till proven otherwise
 - ✚ late complication of scleroderma --> pulmonary hypertension plus/minus fibrosis.
 - ✚ causes of erythema multiforme: lamotrigine
 - ✚ vomiting, abdominal pain, hypothyroidism -> Addisonian crisis (TFT typically abnormal in this setting DO NOT give thyroxine).
 - ✚ mouth/genital ulcers and oligoarthritis -> Behçet's (also eye /SKIN lesions, DVT)
 - ✚ mixed drug overdose most important step -> N-acetylcysteine (time dependent prognosis)
 - ✚ 65. cavernous sinus syndrome - 3rd nerve palsy, proptosis, periorbital swelling, conjunctival injection
 - ✚ asymmetric Parkinson's -> likely to be idiopathic
 - ✚ Obese, NIDDM female with abnormal LFT's -> NASH (non-alcoholic steatotic hepatitis)
 - ✚ fluctuating level of consciousness in elderly plus/minus deterioration --> chronic subdural. Can last even longer than 6 months
 - ✚ Sensitivity --> TP/(TP plus FN) e.g. For SLE - ANA highly Sensitive, anti-Smith ab: highly specific
 - ✚ ipsilateral ataxia, Horner's, contralateral loss pain/temp --> PICA stroke (lateral medullary syndrome of Wallenberg)
 - ✚ renal stones (80% calcium, 10% uric acid, 5% ammonium (proteus), 3% other). Uric acid and cysteine stone are radiolucent.
 - ✚ hyperprolactinemia (galactorrhea, amenorrhea, low FSH/LH) -> D2 antagonists (metoclopramide, chlorpromazine, cimetidine NOT TCA's), pregnancy, PCOS, pit tumor/microadenoma, stress.
 - ✚ Distal, asymmetric arthropathy -> PSORIASIS
 - ✚ episodic headache with tachycardia -> pheochromocytoma
 - ✚ very raised WCC -> ALWAYS think of leukemia.
 - ✚ Diagnosis of CLL --> immunophenotyping NOT cytogenetics, NOT bone marrow
 - ✚ pancytopenia with raised MCV --> check B12/folate first (other causes possible but do this FIRST). Often associated with phenytoin use --> decreased folate
 - ✚ miscarriage, DVT, stroke --> LUPUS anticoagulant --> lifelong anticoagulation
 - ✚ Hb elevated, dec ESR -> polycythemia (2ndry if pO2 low)
 - ✚ anosmia, delayed puberty -> Kallman's syndrome (hypogonadotropic hypogonadism)
 - ✚ diagnosis of PKD -> renal US even if think anorexia nervosa
 - ✚ commonest finding in G6PD hemolysis -> haemoglobinuria
 - ✚ mitral stenosis: loud S1 (soft s1 if severe), opening snap. Immobile valve -> no snap.
 - ✚ Flank pain, urinalysis: blood, protein -> renal vein thrombosis. Causes: nephrotic syndrome, RCC, amyloid, acute pyelonephritis, SLE (antiphospholipid syndrome, which is recurrent thrombosis, fetal loss, dec plt. Usual cause of CNS manifestations associated with LUPUS anticoagulant, anticardiolipin ab)
 - ✚ anemia in the elderly assume GI malignancy
 - ✚ hypothermia, acute renal failure -> rhabdomyolysis (collapse assumed)

- ✚ pain, numbness lateral upper thigh --> meralgia paraesthesia (lateral cutaneous nerve compression usually by inguinal ligament)
- ✚ diagnosis of haemochromatosis: screen with Ferritin, confirm by transferrin saturation, genotyping. If nondiagnostic do liver biopsy 0.3% mortality
- ✚ 40 mg hydrocortisone divided doses (BD) --> 10 mg prednisolone (ie. Prednisolone is x4 stronger)
- ✚ Diphtheria -> exudative pharyngitis, lymphadenopathy, cardio and neuro toxicity.
- ✚ Indurated plaques on cheeks, scarring alopecia, hyperkeratosis over hair follicles --> Discoid LUPUS
- ✚ wt. loss, malabsorption, inc ALP -> pancreatic cancer
- ✚ foreign travel, tender RUQ, raised ALP --> liver abscess do U/S
- ✚ Wt. loss, anemia (macro/micro), no obvious cause -> coeliac (diarrhea does NOT have to be present)
- ✚ haematuria, proteinuria, best investigation --> if glomerulonephritis suspected --> renal biopsy
- ✚ venous ulcer treatment --> exclude arteriopathy (eg ABPI), control edema, prevent infection, compression bandaging.
- ✚ Malaria, incubation within 3/12. can be relapsing /remitting. Vivax and Ovale (West Africa) longer incubation.
- ✚ Fever, lymphadenopathy, lymphocytosis, pharyngitis --->EBV ---> heterophile antibodies
- ✚ GI bleed after endovascular AAA Surgery --> aortoenteric fistula
- ✚ 104. Young girl – suspect Anorexia Nervosa – linugo hair, functional hypogonadotropic hypogonadism -> amenorrhea. LH and FSH both low. All other hormones are usually normal. Ferritin low.
- ✚ Reiter's Syndrome – arthritis, uveitis, urethritis – Chlamydia, campylobacter, Yersinia, SALMONELLA , Shigella. Balanitis.
- ✚ PKD – autosomal dominant Chr 16/4 Associated berry aneurysm, mitral/aortic regurge
- ✚ heart sounds: Aortic Stenosis s2 paradoxical split, length proportional to severity
- ✚ Vitiligo – commonest associations -- pernicious anemia >>> type 1 DM , autoimmune Addison's, autoimmune thyroid diseases
- ✚ CNS abnormalities in HIV: toxoplasmosis (ring enhancing), lymphoma (solitary lesion). HIV encephalopathy, progressive multifocal leukoencephalopathy (PML – demyelination in advanced HIV, low attenuation lesions)
- ✚ Travelers diarrhea: chronic (>2 WEEKS) giardia (insidious onset . (give Metronidazole), SALMONELLA (serious systemic illness), E.coli (give. Ciprofloxacin) , Shigella
- ✚ If you see blood on urinalysis forget about RAS
- ✚ Thyroid Malignancy – tend to be non-functional, anaplastic has worse prognosis, local infiltration -> dysphagia, vocal cord paralysis
- ✚ fatiguability -> myasthenia gravis
- ✚ fasciculations -> Motor neuron disease
- ✚ silvery white scale -> PSORIASIS
- ✚ hypopigmented lesions -> vitiligo/Pityriasis versicolor
- ✚ GBM acts as strong barrier due to – lamina densa
- ✚ A patient of nephrotic syndrome, which structure in GBM plays role in selective permeability of proteins – lamina rara externa
- ✚ Protein filtration of glomerulus is due to – lamina rara interna.

LAB VALUES

Hematology / Blood

RBC	4.5-5.5 Million
Hemoglobin	14-18 g/dL (Men) 12-16 g/dL (Women)
Hematocrit	42-52% (Men) 37-57% (Women)
Platelets	150,000 - 400,000
WBC	4,000 - 10,000

Coagulation

PT	10 -12 second
aPTT	25-35 sec 30-70 sec (heparin)
INR	0.9-1.2 Seconds 2-3 seconds (warfarin)
D-Dimer	<300

Cardiac

Myoglobin	28-72 (M) 25-58 (F)
Troponin I	< 0.1 ng/mL
Troponin T	< 0.03 ng/mL
Creatine Kinase	30-170 U/L

Liver

AST	0-35 U/L
ALT	0-35 U/L
ALP	36-150 U/L
Bilirubin	0-0.8 mg/dL (Total)
Albumin	3.5-5 g/dL
Total protein	6-8 g/dL

Electrolytes

Sodium	Na+	135-145 mEq/L
Potassium	K+	3.5-5 mEq/L
Calcium	Ca	8.5-10.5 mg/dL
Chlorine	Cl-	98-106 mEq/L
Magnesium	Mg	1.3-2.1 mg/dL
Phosphate	PO4	2.5-4.5 mg/dL

Renal

GFR	>90
Creatinine	0.6-1.2 (serum) 90-139 (Clearance)
BUN	10-20 mg/dL

Lipid

Cholesterol	<200
triglycerides	<150
LDL	<130 mg/dL
HDL	>40 mg/dL

Arterial Blood Gas (ABG)

pH	7.35-7.45
PaCO2	35-45 mmHg
HCO3	22-26 mEq/L
SPO2	94-100%
PaO2	80-100 mmHg

Glucose levels

Glucose	70-100 (fasting)
HB A1c	<7%

Pregnancy

Normal	<140 mg/dL
1-hour	<180
2-hour	<155
3-hour	<140

Diabetes (fasting values)

At risk	100-125 mg/dL
Diabetes	126 mg/dL or higher

Various

Alpha fetoprotein	0-20 ng/dL
Chorionic Villus	<5 IU/l
Non stress test	HR >15 BPM for 15 sec W/I (X2 in 20 min)
Fetal Lung Mature	2:1 ratio = mature 2.5 -3 ratio (Diabetes)
Lead	<40 g/dL